

SUPPORT FOR AMENDMENTS

In Claim 1 the description of Ring B has been amended to more clearly conform with the restriction requirement using language disclosed in the specification. Applicants have entered new Claims 25 and 26 based on the scope of Claims 8 and 18, respectively, combined with the structural formula of 2-oxo-1,5-benzodiazepinyl. No new matter will be entered upon entry of this amendment.

REMARKS

Reconsideration and re-examination is respectfully requested.

After entering these amendments, Claims 1-4, 6, 8, 10-14, 16, 18, 20, 22, 23, 25, and 26 will be pending. Claims 1, 3, 4, 6, 8, 10, 11, 13, 14, 16, 18, 20, and 23 have been rewritten. The marked-up version of these amendments is found on a separate sheet attached to this amendment and titled "Marked-Up Version of Rewritten Claims". It is respectfully requested that the amendments above be entered before reexamination of the application.

Rejection under 35 U.S.C §112, second paragraph

Examiner has rejected Claims 15, 16, 18, 20, 23 and 24 for reasons 3f) and 3aa).

3f) Examiner has rejected Claims 15, 16, 18 and 20 for insufficient antecedent basis for the limitation "3 R¹³'s" in the structural formulae of ring B. Applicant has canceled Claim 15 in light of amendments to Claim 14 and amended Claim 14 to provide antecedent basis for the limitation "3 R¹³'s" in the structural formula of ring B. Claims 16, 18 and 20 depend from Claim 14, respectively. In view of the amendment, Applicants respectfully request the rejection be withdrawn.

3aa) Examiner has rejected Claims 23 and 24 as being vague and indefinite. Applicant has amended Claim 23 to more clearly state Alzheimer's Disease. Applicant has canceled Claim 24. Therefore, in light of the amendments Applicants respectfully request the rejection be withdrawn.

Provisional Rejection of Claims under 35 USC §101.

The Examiner has provisionally rejected Claims 5, 6, 8, 10-16, 18 and 20 under 35 U.S.C. §101 as being unpatentable over copending Application No. 09/469,939. Applicants, respectfully, request withdrawal of the provisional rejection on the basis that Application No. 09/469,939 is abandoned.

Provisional Rejection of Claims under the judicially created doctrine of obviousness-type double patenting.

The Examiner has provisionally rejected Claims 1-4 and 22-24 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over copending Application No. 09/469,939. Applicants, respectfully, request withdrawal of the provisional rejection on the basis that Application No. 09/469,939 is abandoned.

Rejection as being drawn to an improper Markush group.

The rejection of Claims 1-5, 10, 12-15, 20 and 22-24 as being drawn to an improper Markush group has been obviated by the present amendments. Withdrawal of this rejection is respectfully requested.

Rejection under 35 U.S.C §112, second paragraph

Examiner has rejected Claims 5, 6, 15, and 16 for reasons a) through d).

a) Examiner has rejected Claim 5 for lack of antecedent basis in the limitation "R¹¹ substituted to a seven membered ring" in the third structural formula of the second

row. Withdrawal of this rejection is respectfully requested on the basis that Claim 5 has been canceled.

b) Examiner has rejected Claim 6 for lack of antecedent basis in the limitation "R¹¹ substituted to a seven membered ring" in the structural formula in the claim. Applicant's traverse the rejection.

Applicants disclose that "Ring B is a 7 membered lactam ... wherein each additional lactam carbon ... is substituted with 0-2 R¹¹...." (Claim 1, p183; et seq.) In the specification, page 92, Applicants teach what an "additional lactam carbon" is and provide examples of "R¹¹ substituted to a seven membered ring". More specifically Applicants teach R¹¹ substituted to a 2-oxo-1,4-benzodiazepinyl ring in Example B6 (page 93). Therefore, Applicants submit that there is antecedent basis in Claims 1-4 for the limitation "R¹¹ substituted to a seven membered ring" in the structural formula in Claim 6.

In view of the amendment, Applicant respectfully requests the rejection be withdrawn.

c) Examiner has rejected Claim 15 for lack of antecedent basis in the limitation "R¹¹ substituted to a seven membered ring" in the third structural formula of the second row. Applicant's traverse the rejection. Withdrawal of this rejection is respectfully requested on the basis that Claim 5 has been canceled.

d) Examiner has rejected Claim 16 for lack of antecedent basis in the limitation "R¹¹ substituted to a seven membered ring" in the structural formula in the claim. Applicant's traverse the rejection.

For the reason stated in b) above Applicants submit that there is antecedent basis in Claims 11-14 for the

Amendment & Response – Docket No. DM-7076-A
Serial No.: 09/505,788
Date: April 10, 2002

limitation "R¹¹ substituted to a seven membered ring" in the structural formula in Claim 16.

In view of the amendment, Applicant respectfully requests the rejection be withdrawn.

CONCLUSION

The claims of the present invention have been amended to place the Application in form for Allowance. In view of the foregoing, Applicants submit that the application is now in condition for allowance. Reconsideration and allowance is respectfully requested. Notification of such action is earnestly solicited.

Respectfully submitted,



Scott K. Larsen, Ph.D. J.D.
Attorney for Applicants
Registration No. 38,532
Telephone 302/467-5261

Bristol-Myers Squibb Company
P.O. Box 4000, Patent Dept.
Princeton, N.J. 08543-4000

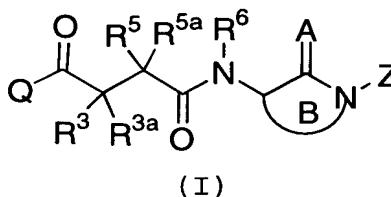
Marked-Up Version of Rewritten Claims 1, 3, 4, 6, 8, 10, 11, 13, 14, 16, 18, 20, and 23.

Docket No. PH-7076-A

Serial No.: 09/505,788

The subject matter to be added is in **bold and underlined** and the subject matter to be deleted is in **bold and has been bracketed []** with square brackets.

1. (Twice Amended) A compound of Formula (I) :



or a pharmaceutically acceptable salt thereof, wherein:

A is O or S;

Q is -NR¹R²;

R¹ is selected from: H and C₁-C₆ alkyl;

[H;

C₁-C₆ alkyl substituted with 0-3 R^{1a};

C₃-C₁₀ carbocycle substituted with 0-3 R^{1b};

C₆-C₁₀ aryl substituted with 0-3 R^{1b}; and

5 to 10 membered heterocycle containing 1 to 4

heteroatoms selected from nitrogen, oxygen, and

sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{1b};

R^{1a}, at each occurrence, is independently selected from H,

C₁-C₆ alkyl, Cl, F, Br, I, =O, CN, NO₂, NR¹⁵R¹⁶, CF₃;

C₃-C₁₀ carbocycle substituted with 0-3 R^{1b};

C₆-C₁₀ aryl substituted with 0-3 R^{1b}; and

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{1b};

R^{1b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₆ haloalkyl, and C₁-C₄ haloalkoxy;

R² is independently selected from H [,] and C₁-C₆ alkyl[, C₃-C₁₀ carbocycle, C₆-C₁₀ aryl, and 5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur];

R³ is -(CR⁷R^{7a})_n-R⁴,
-(CR⁷R^{7a})_n-S-(CR⁷R^{7a})_m-R⁴,
-(CR⁷R^{7a})_n-O-(CR⁷R^{7a})_m-R⁴,
-(CR⁷R^{7a})_n-N(R^{7b})-(CR⁷R^{7a})_m-R⁴,
-(CR⁷R^{7a})_n-S(=O)-(CR⁷R^{7a})_m-R⁴,
-(CR⁷R^{7a})_n-S(=O)₂-(CR⁷R^{7a})_m-R⁴,
-(CR⁷R^{7a})_n-C(=O)-(CR⁷R^{7a})_m-R⁴,
-(CR⁷R^{7a})_n-N(R^{7b})C(=O)-(CR⁷R^{7a})_m-R⁴,
-(CR⁷R^{7a})_n-C(=O)N(R^{7b})-(CR⁷R^{7a})_m-R⁴,
-(CR⁷R^{7a})_n-N(R^{7b})S(=O)₂-(CR⁷R^{7a})_m-R⁴, or
-(CR⁷R^{7a})_n-S(=O)₂N(R^{7b})-(CR⁷R^{7a})_m-R⁴;

n is 0, 1, 2, or 3;

m is 0, 1, 2, or 3;

R^{3a} is H, OH, C₁-C₄ alkyl, C₁-C₄ alkoxy, C₂-C₄ alkenyl or C₂-C₄ alkenyloxy;

R⁴ is H, OH, OR^{14a},
C₁-C₆ alkyl substituted with 0-3 R^{4a},
C₂-C₆ alkenyl substituted with 0-3 R^{4a},
C₂-C₆ alkynyl substituted with 0-3 R^{4a},

C₃-C₁₀ carbocycle substituted with 0-3 R^{4b},
C₆-C₁₀ aryl substituted with 0-3 R^{4b}, or
5 to 10 membered heterocycle containing 1 to 4
heteroatoms selected from nitrogen, oxygen, and
sulphur, wherein said 5 to 10 membered heterocycle is
substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from[is]
H, F, Cl, Br, I, CF₃,
C₃-C₁₀ carbocycle substituted with 0-3 R^{4b},
C₆-C₁₀ aryl substituted with 0-3 R^{4b}, or
5 to 10 membered heterocycle containing 1 to 4
heteroatoms selected from nitrogen, oxygen, and
sulphur, wherein said 5 to 10 membered heterocycle is
substituted with 0-3 R^{4b};

R^{4b}, at each occurrence, is independently selected from H, OH,
Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃,
S(=O)CH₃, S(=O)₂CH₃,
C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl,
C₁-C₄ haloalkoxy, and C₁-C₄ haloalkyl-S-;

R⁵ is H, OR¹⁴;
C₁-C₆ alkyl substituted with 0-3 R^{5b};
C₁-C₆ alkoxy substituted with 0-3 R^{5b};
C₂-C₆ alkenyl substituted with 0-3 R^{5b};
C₂-C₆ alkynyl substituted with 0-3 R^{5b};
C₃-C₁₀ carbocycle substituted with 0-3 R^{5c};
C₆-C₁₀ aryl substituted with 0-3 R^{5c}; or
5 to 10 membered heterocycle containing 1 to 4
heteroatoms selected from nitrogen, oxygen, and
sulphur, wherein said 5 to 10 membered heterocycle is
substituted with 0-3 R^{5c};

R^{5a} is H, OH, C₁-C₄ alkyl, C₁-C₄ alkoxy, C₂-C₄ alkenyl, or C₂-
C₄ alkenyloxy;

R^{5b}, at each occurrence, is independently selected from:
H, C₁-C₆ alkyl, CF₃, OR¹⁴, Cl, F, Br, I, =O, CN, NO₂,
NR¹⁵R¹⁶;
C₃-C₁₀ carbocycle substituted with 0-3 R^{5c};
C₆-C₁₀ aryl substituted with 0-3 R^{5c}; or
5 to 10 membered heterocycle containing 1 to 4
heteroatoms selected from nitrogen, oxygen, and
sulphur, wherein said 5 to 10 membered heterocycle is
substituted with 0-3 R^{5c};

R^{5c}, at each occurrence, is independently selected from H, OH,
Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃,
S(=O)CH₃, S(=O)₂CH₃,
C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl,
C₁-C₄ haloalkoxy, and C₁-C₄ haloalkyl-S-;

R⁶ is H;
C₁-C₆ alkyl substituted with 0-3 R^{6a};
C₃-C₁₀ carbocycle substituted with 0-3 R^{6b}; or
C₆-C₁₀ aryl substituted with 0-3 R^{6b};

R^{6a}, at each occurrence, is independently selected from H,
C₁-C₆ alkyl, OR¹⁴, Cl, F, Br, I, =O, CN, NO₂, NR¹⁵R¹⁶,
aryl or CF₃;

R^{6b}, at each occurrence, is independently selected from H, OH,
Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, C₁-C₆ alkyl, C₁-C₄
alkoxy, C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

R⁷, at each occurrence, is independently selected from H, OH,
Cl, F, Br, I, CN, NO₂, CF₃, phenyl and C₁-C₄ alkyl;

R^{7a}, at each occurrence, is independently selected from H, OH,
Cl, F, Br, I, CN, NO₂, CF₃, and C₁-C₄ alkyl;

R^{7b} is independently selected from H and C₁-C₄ alkyl;

Ring B is a 7 membered lactam or thiolactam,
wherein the lactam is 2-oxo-azepinyl or thiolactam is 2-thioxo-azepinyl [saturated, partially saturated or unsaturated];
wherein each additional lactam carbon or thiolactam carbon is substituted with 0-2 R¹¹; provided two R¹¹ substituents are present on adjacent atoms and are combined to form a benzo fused radical; wherein said benzo fused radical is substituted with 0-4 R¹³;
and,
wherein [optionally,] the lactam or thiolactam contains a heteroatom selected from [-O-, -S-, -S(=O)-, -S(=O)₂-,] -N=, -NH-, and -N(R¹⁰)-;

[additionally, two R¹¹ substituents on adjacent atoms may be combined to form a benzo fused radical; wherein said benzo fused radical is substituted with 0-4 R¹³;

additionally, two R¹¹ substituents on adjacent atoms may be combined to form a 5 to 6 membered heteroaryl fused radical, wherein said 5 to 6 membered heteroaryl fused radical comprises 1 or 2 heteroatoms selected from N, O, and S; wherein said 5 to 6 membered heteroaryl fused radical is substituted with 0-3 R¹³;

additionally, two R¹¹ substituents on the same or adjacent carbon atoms may be combined to form a C₃-C₆ carbocycle substituted with 0-3 R¹³;]

R¹⁰ is H, C(=O)R¹⁷, C(=O)OR¹⁷, C(=O)NR¹⁸R¹⁹, S(=O)₂NR¹⁸R¹⁹, S(=O)₂R¹⁷;

C₁-C₆ alkyl optionally substituted with 0-3 R^{10a};

C₆-C₁₀ aryl substituted with 0-4 R^{10b};

C₃-C₁₀ carbocycle substituted with 0-3 R^{10b}; or

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and

sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{10b};

R^{10a}, at each occurrence, is independently selected from H, C₁-C₆ alkyl, OR¹⁴, Cl, F, Br, I, =O, CN, NO₂, NR¹⁵R¹⁶, CF₃, or aryl substituted with 0-4 R^{10b};

R^{10b}, at each occurrence, is independently selected from H, OH, C₁-C₆ alkyl, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, and C₁-C₄ haloalkyl-S-;

R¹¹, at each occurrence, is independently selected from H, C₁-C₄ alkoxy, Cl, F, Br, I, =O, CN, NO₂, NR¹⁸R¹⁹, C(=O)R¹⁷, C(=O)OR¹⁷, C(=O)NR¹⁸R¹⁹, S(=O)₂NR¹⁸R¹⁹, CF₃; C₁-C₆ alkyl optionally substituted with 0-3 R^{11a}; C₆-C₁₀ aryl substituted with 0-3 R^{11b}; C₃-C₁₀ carbocycle substituted with 0-3 R^{11b}; or 5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{11b};

R^{11a}, at each occurrence, is independently selected from H, C₁-C₆ alkyl, OR¹⁴, Cl, F, Br, I, =O, CN, NO₂, NR¹⁵R¹⁶, CF₃; phenyl substituted with 0-3 R^{11b}; C₃-C₆ cycloalkyl substituted with 0-3 R^{11b}; and 5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃,

C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl,
C₁-C₄ haloalkoxy, and C₁-C₄ haloalkyl-S-;

Z is H;

C₁-C₈ alkyl substituted with 1-3 R¹²;
C₂-C₄ alkenyl substituted with 1-3 R¹²;
C₂-C₄ alkynyl substituted with 1-3 R¹²;
C₁-C₈ alkyl substituted with 0-3 R^{12a};
C₂-C₄ alkenyl substituted with 0-3 R^{12a};
C₂-C₄ alkynyl substituted with 0-3 R^{12a};
C₆-C₁₀ aryl substituted with 0-4 R^{12b};
C₃-C₁₀ carbocycle substituted with 0-4 R^{12b}; or
5 to 10 membered heterocycle containing 1 to 4
heteroatoms selected from nitrogen, oxygen, and
sulphur, wherein said 5 to 10 membered heterocycle is
substituted with 0-3 R^{12b};

R¹², at each occurrence, is independently selected from
C₆-C₁₀ aryl substituted with 0-4 R^{12b};
C₃-C₁₀ carbocycle substituted with 0-4 R^{12b}; or
5 to 10 membered heterocycle containing 1 to 4
heteroatoms selected from nitrogen, oxygen, and
sulphur, wherein said 5 to 10 membered heterocycle is
substituted with 0-3 R^{12b};

R^{12a}, at each occurrence, is independently selected from
H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, -C(=O)NR¹⁵R¹⁶, CF₃,
acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃,
C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl,
C₁-C₄ haloalkoxy, or C₁-C₄ haloalkyl-S-;

R^{12b}, at each occurrence, is independently selected from
H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃,
S(=O)CH₃, S(=O)₂CH₃,
C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl,
C₁-C₄ haloalkoxy, and C₁-C₄ haloalkyl-S-;

R¹³, at each occurrence, is independently selected from
H, OH, C₁-C₆ alkyl, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO₂,
NR¹⁵R¹⁶, and CF₃;

R¹⁴ is H, phenyl, benzyl, C₁-C₆ alkyl, C₂-C₆ alkoxyalkyl, or
C₃-C₆ cycloalkyl;

R^{14a} is H, phenyl, benzyl, or C₁-C₄ alkyl;

R¹⁵, at each occurrence, is independently selected from H, C₁-
C₆ alkyl, benzyl, phenethyl, (C₁-C₆ alkyl)-C(=O)-, and
(C₁-C₆ alkyl)-S(=O)₂-;

R¹⁶, at each occurrence, is independently selected from
H, OH, C₁-C₆ alkyl, benzyl, phenethyl,
(C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-;

R¹⁷ is H, C₁-C₆ alkyl, C₂-C₆ alkoxyalkyl,
aryl substituted by 0-4 R^{17a}, or
-CH₂-aryl substituted by 0-4 R^{17a};

R^{17a} is H, methyl, ethyl, propyl, butyl, methoxy, ethoxy,
propoxy, butoxy, -OH, F, Cl, Br, I, CF₃, OCF₃, SCH₃,
S(O)CH₃, SO₂CH₃, -NH₂, -N(CH₃)₂, or C₁-C₄ haloalkyl;

R¹⁸, at each occurrence, is independently selected from
H, C₁-C₆ alkyl, phenyl, benzyl, phenethyl,
(C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-; and

R¹⁹, at each occurrence, is independently selected from
H, OH, C₁-C₆ alkyl, phenyl, benzyl, phenethyl,
(C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-;

provided, when R¹³ is H,
then Z is H;

C₄-C₈ alkyl substituted with 1-3 R¹²;
C₂-C₄ alkenyl substituted with 1-3 R¹²;

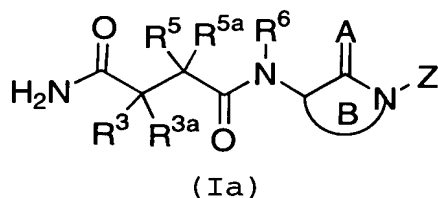
C₂-C₄ alkynyl substituted with 1-3 R¹²;
C₁-C₈ alkyl substituted with 0-3 R^{12a};
C₂-C₄ alkenyl substituted with 0-3 R^{12a}; or
C₂-C₄ alkynyl substituted with 0-3 R^{12a}; and

provided, when ring B is a 1,3,4,5-tetrahydro-1-(Z)-5-(R¹⁰)-6,6,7,7-tetra(R¹¹)-2,4-dioxo-2H-1,5-diazepin-3-yl core, and R¹³ is H; then

R¹⁰ is H, C(=O)R¹⁷, C(=O)OR¹⁷, C(=O)NR¹⁸R¹⁹,
S(=O)₂NR¹⁸R¹⁹, S(=O)₂R¹⁷; or
C₁-C₆ alkyl optionally substituted with 0-3 R^{10a};

R^{10a}, at each occurrence, is independently selected from
H, C₁-C₆ alkyl, OR¹⁴, Cl, F, Br, I, =O, CN, NO₂, NR¹⁵R¹⁶,
and CF₃.

2. (Amended) A compound, according to Claim 1, of Formula
(Ia):



or a pharmaceutically acceptable salt thereof,
wherein:

Z is H;
C₁-C₈ alkyl substituted with 0-3 R^{12a};
C₂-C₄ alkenyl substituted with 0-3 R^{12a}; or
C₂-C₄ alkynyl substituted with 0-3 R^{12a}.

3. (Amended) A compound according to Claim 2 of Formula
(Ia)



(Ia)

or a pharmaceutically acceptable salt thereof,
 wherein:

R³ is -(CR⁷R^{7a})_n-R⁴,
 -(CR⁷R^{7a})_n-S-(CR⁷R^{7a})_m-R⁴,
 -(CR⁷R^{7a})_n-O-(CR⁷R^{7a})_m-R⁴, or
 -(CR⁷R^{7a})_n-N(R^{7b})-(CR⁷R^{7a})_m-R⁴;

n is 0, 1, or 2;

m is 0, 1, or 2;

R^{3a} is H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy,
 propoxy, butoxy, allyl, or 3-buten-1-yl;

R⁴ is H, OH, OR^{14a},
 C₁-C₆ alkyl substituted with 0-3 R^{4a},
 C₂-C₆ alkenyl substituted with 0-3 R^{4a},
 C₂-C₆ alkynyl substituted with 0-3 R^{4a},
 C₃-C₁₀ carbocycle substituted with 0-3 R^{4b},
 C₆-C₁₀ aryl substituted with 0-3 R^{4b}, or
 5 to 10 membered heterocycle containing 1 to 4
 heteroatoms selected from nitrogen, oxygen, and
 sulphur, wherein said 5 to 10 membered heterocycle is
 substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from **[is]**
 H, F, Cl, Br, I, CF₃,
 C₃-C₁₀ carbocycle substituted with 0-3 R^{4b},
 C₆-C₁₀ aryl substituted with 0-3 R^{4b}, or
 5 to 10 membered heterocycle containing 1 to 4
 heteroatoms selected from nitrogen, oxygen, and

sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b};

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

R⁵ is H, OR¹⁴;

C₁-C₆ alkyl substituted with 0-3 R^{5b};

C₁-C₆ alkoxy substituted with 0-3 R^{5b};

C₂-C₆ alkenyl substituted with 0-3 R^{5b};

C₂-C₆ alkynyl substituted with 0-3 R^{5b};

C₃-C₁₀ carbocycle substituted with 0-3 R^{5c};

C₆-C₁₀ aryl substituted with 0-3 R^{5c}; or

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c};

R^{5a} is H or C₁-C₄ alkyl;

R^{5b}, at each occurrence, is independently selected from:

H, C₁-C₆ alkyl, CF₃, OR¹⁴, Cl, F, Br, I, =O, CN, NO₂, NR¹⁵R¹⁶;

C₃-C₁₀ carbocycle substituted with 0-3 R^{5c};

C₆-C₁₀ aryl substituted with 0-3 R^{5c}; or

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c};

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

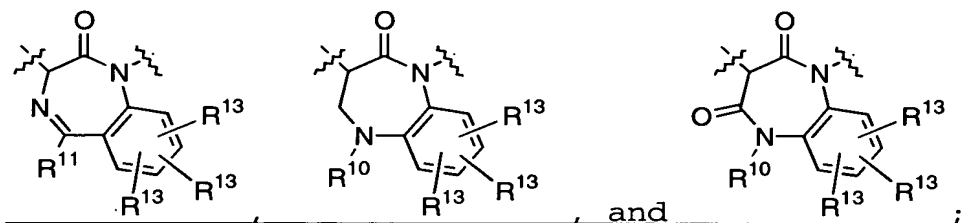
R⁶ is H, methyl, or ethyl;

R⁷, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, CF₃, phenyl and C₁-C₄ alkyl;

R^{7a}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, CF₃, and C₁-C₄ alkyl;

R^{7b} is independently selected from H, methyl, ethyl, propyl, and butyl;

Ring B is selected from



[a 7 membered lactam or thiolactam,
wherein the lactam or thiolactam is saturated, partially
saturated or unsaturated;
wherein each additional lactam carbon or thiolactam
carbon is substituted with 0-2 R¹¹; and,
optionally, the lactam or thiolactam contains a
heteroatom selected from, -O-, -S-, -S(=O)-, -S(=O)₂-,
-N=, -NH-, and -N(R¹⁰)-;

additionally, two R¹¹ substituents on adjacent atoms may be
combined to form a benzo fused radical; wherein said
benzo fused radical is substituted with 0-3 R¹³;

additionally, two R¹¹ substituents on adjacent atoms may be
combined to form a 5 to 6 membered heteroaryl fused
radical, wherein said 5 to 6 membered heteroaryl fused
radical comprises 1 or 2 heteroatoms selected from N, O,

and S; wherein said 5 to 6 membered heteroaryl fused radical is substituted with 0-3 R¹³;

additionally, two R¹¹ substituents on the same or adjacent carbon atoms may be combined to form a C₃-C₆ carbocycle substituted with 0-3 R¹³;

R¹⁰ is H, C(=O)R¹⁷, C(=O)OR¹⁷, C(=O)NR¹⁸R¹⁹, S(=O)₂NR¹⁸R¹⁹, S(=O)₂R¹⁷;
C₁-C₆ alkyl optionally substituted with 0-2 R^{10a};
C₆-C₁₀ aryl substituted with 0-4 R^{10b};
C₃-C₁₀ carbocycle substituted with 0-3 R^{10b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{10b};

R^{10a}, at each occurrence, is independently selected from H, C₁-C₆ alkyl, OR¹⁴, Cl, F, Br, I, =O, CN, NO₂, NR¹⁵R¹⁶, CF₃, or phenyl substituted with 0-4 R^{10b};

R^{10b}, at each occurrence, is independently selected from H, OH, C₁-C₆ alkyl, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, or CF₃;

R¹¹, at each occurrence, is independently selected from H, C₁-C₄ alkoxy, Cl, F, Br, I, [=O,] CN, NO₂, NR¹⁸R¹⁹, C(=O)R¹⁷, C(=O)OR¹⁷, C(=O)NR¹⁸R¹⁹, S(=O)₂NR¹⁸R¹⁹, CF₃;
C₁-C₆ alkyl optionally substituted with 0-3 R^{11a};
C₆-C₁₀ aryl substituted with 0-3 R^{11b};
C₃-C₁₀ carbocycle substituted with 0-3 R^{11b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{11b};

R^{11a}, at each occurrence, is independently selected from H, C₁-C₆ alkyl, OR¹⁴, Cl, F, Br, I, =O, CN, NO₂, NR¹⁵R¹⁶, CF₃, or phenyl substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

Z is H;

C₁-C₆ alkyl substituted with 0-3 R^{12a};
C₂-C₄ alkenyl substituted with 0-3 R^{12a}; or
C₂-C₄ alkynyl substituted with 0-3 R^{12a};

R^{12a}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

R¹³, at each occurrence, is independently selected from H, OH, C₁-C₆ alkyl, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, and CF₃;

R¹⁴ is H, phenyl, benzyl, C₁-C₆ alkyl, or C₂-C₆ alkoxyalkyl;

R^{14a} is H, phenyl, benzyl, methyl, ethyl, propyl, or butyl;

R¹⁵, at each occurrence, is independently selected from H, C₁-C₆ alkyl, benzyl, phenethyl, (C₁-C₆ alkyl)-C(=O)-; and (C₁-C₆ alkyl)-S(=O)₂-;

R¹⁶, at each occurrence, is independently selected from H, OH, C₁-C₆ alkyl, benzyl, phenethyl, (C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-;

R¹⁷ is H, C₁-C₆ alkyl, C₂-C₆ alkoxyalkyl, aryl substituted by 0-4 R^{17a}, or

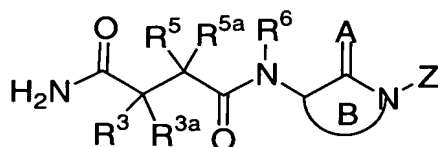
-CH₂-aryl substituted by 0-4 R^{17a};

R^{17a} is H, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, -OH, F, Cl, Br, I, CF₃, OCF₃, SCH₃, S(O)CH₃, SO₂CH₃, -NH₂, -N(CH₃)₂, or C₁-C₄ haloalkyl;

R¹⁸, at each occurrence, is independently selected from H, C₁-C₆ alkyl, phenyl, benzyl, phenethyl, (C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-; and

R¹⁹, at each occurrence, is independently selected from H, OH, C₁-C₆ alkyl, phenyl, benzyl, phenethyl, (C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-.

4. (Twice Amended) A compound according to Claim 3 of Formula (Ia)



(Ia)

or a pharmaceutically acceptable salt thereof,

wherein:

R³ is -(CHR⁷)_n-R⁴,

n is 0 or 1;

R^{3a} is H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, allyl, or 3-buten-1-yl;

R⁴ is H, OH, OR^{14a},

C₁-C₄ alkyl substituted with 0-2 R^{4a},

C₂-C₄ alkenyl substituted with 0-2 R^{4a},

C₂-C₄ alkynyl substituted with 0-1 R^{4a},

C₃-C₆ carbocycle substituted with 0-3 R^{4b},
C₆-C₁₀ aryl substituted with 0-3 R^{4b}, or
5 to 6 membered heterocycle containing 1 to 4
heteroatoms selected from nitrogen, oxygen, and
sulphur, wherein said 5 to 6 membered heterocycle is
substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from **[is]**
H, F, Cl, Br, I, CF₃,
C₃-C₆ carbocycle substituted with 0-3 R^{4b},
phenyl substituted with 0-3 R^{4b}, or
5 to 6 membered heterocycle containing 1 to 4
heteroatoms selected from nitrogen, oxygen, and
sulphur, wherein said 5 to 6 membered heterocycle is
substituted with 0-3 R^{4b};

R^{4b}, at each occurrence, is independently selected from H, OH,
Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃,
S(=O)CH₃, S(=O)₂CH₃, C₁-C₄ alkyl, C₁-C₃ alkoxy, C₁-C₂
haloalkyl, and C₁-C₂ haloalkoxy;

R⁵ is H, OR¹⁴;
C₁-C₄ alkyl substituted with 0-3 R^{5b};
C₂-C₄ alkenyl substituted with 0-3 R^{5b};
C₂-C₄ alkynyl substituted with 0-3 R^{5b};

R^{5a} is H, methyl, ethyl, propyl, or butyl;

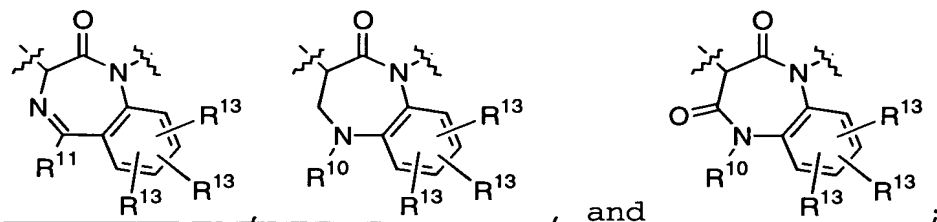
R^{5b}, at each occurrence, is independently selected from:
H, methyl, ethyl, propyl, butyl, CF₃, OR¹⁴, Cl, F, Br, I,
=O;
C₃-C₆ carbocycle substituted with 0-3 R^{5c};
phenyl substituted with 0-3 R^{5c}; or
5 to 6 membered heterocycle containing 1 to 4
heteroatoms selected from nitrogen, oxygen, and
sulphur, wherein said 5 to 6 membered heterocycle is
substituted with 0-3 R^{5c};

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₄ alkyl, C₁-C₃ alkoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R⁶ is H;

R⁷, at each occurrence, is independently selected from H, F, CF₃, methyl, and ethyl;

Ring B is selected from



[a 7 membered lactam or thiolactam,
wherein the lactam or thiolactam is saturated, partially saturated or
unsaturated;

wherein each additional lactam carbon or thiolactam
carbon is substituted with 0-2 R¹¹; and,
optionally, the lactam or thiolactam contains a
heteroatom selected from -N=, -NH-, and -N(R¹⁰)-;

additionally, two R¹¹ substituents on adjacent atoms may be
combined to form a benzo fused radical; wherein said
benzo fused radical is substituted with 0-2 R¹³;

additionally, two R¹¹ substituents on adjacent atoms may be
combined to form a 5 to 6 membered heteroaryl fused
radical, wherein said 5 to 6 membered heteroaryl fused
radical comprises 1 or 2 heteroatoms selected from N, O,
and S; wherein said 5 to 6 membered heteroaryl fused
radical is substituted with 0-2 R¹³;

additionally, two R¹¹ substituents on the same or adjacent carbon atoms may be combined to form a C₃-C₆ carbocycle substituted with 0-2 R¹³;

R¹⁰ is H, C(=O)R¹⁷, C(=O)OR¹⁷;
C₁-C₄ alkyl optionally substituted with 0-1 R^{10a};
phenyl substituted with 0-4 R^{10b};
C₃-C₆ carbocycle substituted with 0-3 R^{10b}; or
5 to 6 membered heterocycle containing 1 to 4
heteroatoms selected from nitrogen, oxygen, and
sulphur, wherein said 5 to 6 membered heterocycle is
substituted with 0-3 R^{10b};

R^{10a} **[, at each occurrence,]** is **[independently]** selected from
H, C₁-C₄ alkyl, OR¹⁴, Cl, F, Br, I, =O, CN, NO₂, NR¹⁵R¹⁶,
CF₃, or phenyl substituted with 0-4 R^{10b};

R^{10b}, at each occurrence, is independently selected from H,
OH, C₁-C₄ alkyl, C₁-C₃ alkoxy, Cl, F, Br, I, CN, NO₂,
NR¹⁵R¹⁶, or CF₃;

R¹¹ **[, at each occurrence,]** is **[independently]** selected from
H, C₁-C₄ alkoxy, Cl, F, **[=O,]** NR¹⁸R¹⁹, C(=O)R¹⁷,
C(=O)OR¹⁷, CF₃;
C₁-C₆ alkyl optionally substituted with 0-3 R^{11a};
C₆-C₁₀ aryl substituted with 0-3 R^{11b};
C₃-C₆**[6]** carbocycle substituted with 0-3 R^{11b}; or
5 to 6 membered heterocycle containing 1 to 4
heteroatoms selected from nitrogen, oxygen, and
sulphur, wherein said 5 to 6 membered heterocycle is
substituted with 0-3 R^{11b};

R^{11a}, at each occurrence, is independently selected from H,
C₁-C₄ alkyl, OR¹⁴, F, =O, NR¹⁵R¹⁶, CF₃, or phenyl
substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, C₁-C₄ alkyl, C₁-C₃ alkoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

Z is H;

C₁-C₄ alkyl substituted with 0-3 R^{12a};

C₂-C₄ alkenyl substituted with 0-3 R^{12a}; or

C₂-C₄ alkynyl substituted with 0-3 R^{12a};

R^{12a}, at each occurrence, is independently selected from H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₄ alkyl, C₁-C₃ alkoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R¹³, at each occurrence, is independently selected from H, OH, C₁-C₆ alkyl, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, and CF₃;

R¹⁴ is H, phenyl, benzyl, C₁-C₄ alkyl, or C₂-C₄ alkoxyalkyl;

R¹⁵, at each occurrence, is independently selected from H, C₁-C₄ alkyl, benzyl, phenethyl, (C₁-C₄ alkyl)-C(=O)-, and (C₁-C₄ alkyl)-S(=O)₂-;

R¹⁶, at each occurrence, is independently selected from H, OH, C₁-C₄ alkyl, benzyl, phenethyl, (C₁-C₄ alkyl)-C(=O)-, and (C₁-C₄ alkyl)-S(=O)₂-;

R¹⁷ is H, methyl, ethyl, propyl, butyl, methoxymethyl, ethoxymethyl, methoxyethyl, ethoxyethyl, phenyl substituted by 0-3 R^{17a}, or -CH₂-phenyl substituted by 0-3 R^{17a};

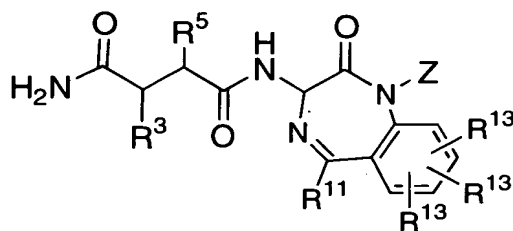
R^{17a} is H, methyl, methoxy, -OH, F, Cl, CF₃, or OCF₃;

R¹⁸, at each occurrence, is independently selected from

H, methyl, ethyl, propyl, butyl, phenyl, benzyl, and phenethyl; and

R¹⁹, at each occurrence, is independently selected from H, methyl, and ethyl.

6. (Twice Amended) A compound according to Claim 4 [5] of Formula (Ic):



(Ic)

or a pharmaceutically acceptable salt thereof
wherein

R³ is R⁴,

R⁴ is C₁-C₄ alkyl substituted with 0-1 R^{4a},
C₂-C₄ alkenyl substituted with 0-1 R^{4a}, or
C₂-C₄ alkynyl substituted with 0-1 R^{4a};

R^{4a} [, at each occurrence,] is [independently] selected from
H, F, CF₃,
C₃-C₆ carbocycle substituted with 0-3 R^{4b},
phenyl substituted with 0-3 R^{4b}, or
5 to 6 membered heterocycle containing 1 to 4
heteroatoms selected from nitrogen, oxygen, and
sulphur, wherein said 5 to 6 membered heterocycle is
substituted with 0-3 R^{4b}; wherein said 5 to 6 membered
heterocycle is selected from pyridinyl, pyrimidinyl,
triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl,
piperazinyl, piperidinyl, pyrazolyl, imidazolyl,
oxazolyl, isoxazolyl, and tetrazolyl;

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R⁵ is C₁-C₄ alkyl substituted with 0-1 R^{5b};
C₂-C₄ alkenyl substituted with 0-1 R^{5b};
C₂-C₄ alkynyl substituted with 0-1 R^{5b};

R^{5b}[, at each occurrence,] is [independently] selected from:
H, methyl, ethyl, propyl, butyl, CF₃, OR¹⁴, =O;
C₃-C₆ carbocycle substituted with 0-2 R^{5c};
phenyl substituted with 0-3 R^{5c}; or
5 to 6 membered heterocycle containing 1 to 4
heteroatoms selected from nitrogen, oxygen, and
sulphur, wherein said 5 to 6 membered heterocycle is
substituted with 0-3 R^{5c}; wherein said 5 to 6 membered
heterocycle is selected from pyridinyl, pyrimidinyl,
triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl,
piperazinyl, piperidinyl, pyrazolyl, imidazolyl,
oxazolyl, isoxazolyl, and tetrazolyl;

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R¹¹[, at each occurrence,] is [independently] selected from
H, [=O,] NR¹⁸R¹⁹, CF₃;
C₁-C₄ alkyl optionally substituted with 0-1 R^{11a};
phenyl substituted with 0-3 R^{11b};
C₃-C₆ carbocycle substituted with 0-3 R^{11b}; and
5 to 6 membered heterocycle containing 1 to 4
heteroatoms selected from nitrogen, oxygen, and
sulphur, wherein said 5 to 6 membered heterocycle is
substituted with 0-3 R^{11b}; wherein said 5 to 6

membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{11a} [, at each occurrence,] is [independently] selected from H, C₁-C₄ alkyl, OR¹⁴, F, [C1,] =O, NR¹⁵R¹⁶, CF₃, or phenyl substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

Z is H;

C₁-C₄ alkyl substituted with 0-3 R^{12a};

C₂-C₄ alkenyl substituted with 0-3 R^{12a}; or

C₂-C₄ alkynyl substituted with 0-3 R^{12a};

R^{12a}, at each occurrence, is independently selected from H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R¹³, at each occurrence, is independently selected from H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, Cl, F, Br, CN, NR¹⁵R¹⁶, and CF₃;

R¹⁴ is H, phenyl, benzyl, methyl, ethyl, propyl, or butyl;

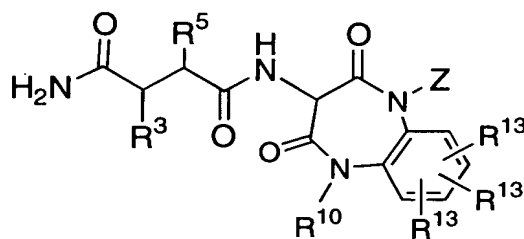
R¹⁵, at each occurrence, is independently selected from H, methyl, ethyl, propyl, and butyl;

R¹⁶, at each occurrence, is independently selected from H, OH, methyl, ethyl, propyl, butyl, benzyl, phenethyl, methyl-C(=O)-, ethyl-C(=O)-, methyl-S(=O)₂-, and ethyl-S(=O)₂-;

R¹⁸, at each occurrence, is independently selected from H, methyl, ethyl, propyl, butyl, phenyl, benzyl, and phenethyl; and

R¹⁹, at each occurrence, is independently selected from H, methyl, and ethyl.

8. (Twice Amended) A compound according to Claim 4 [5] of Formula (Ie):



(Ie)

or a pharmaceutically acceptable salt thereof wherein:

R³ is R⁴,

R⁴ is C₁-C₄ alkyl substituted with 0-1 R^{4a},
C₂-C₄ alkenyl substituted with 0-1 R^{4a}, or
C₂-C₄ alkynyl substituted with 0-1 R^{4a};

R^{4a} [, at each occurrence,] is [independently] selected from
H, F, CF₃,
C₃-C₆ carbocycle substituted with 0-3 R^{4b},
phenyl substituted with 0-3 R^{4b}, or
5 to 6 membered heterocycle containing 1 to 4
heteroatoms selected from nitrogen, oxygen, and
sulphur, wherein said 5 to 6 membered heterocycle is
substituted with 0-3 R^{4b}; wherein said 5 to 6 membered
heterocycle is selected from pyridinyl, pyrimidinyl,
triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl,

piperazinyl, piperidinyl, pyrazolyl, imidazolyl,
oxazolyl, isoxazolyl, and tetrazolyl;

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R⁵ is C₁-C₄ alkyl substituted with 0-1 R^{5b};
C₂-C₄ alkenyl substituted with 0-1 R^{5b};
C₂-C₄ alkynyl substituted with 0-1 R^{5b};

R^{5b}[, at each occurrence,] is [independently] selected from:
H, methyl, ethyl, propyl, butyl, CF₃, OR¹⁴, =O;
C₃-C₆ carbocycle substituted with 0-2 R^{5c};
phenyl substituted with 0-3 R^{5c}; or
5 to 6 membered heterocycle containing 1 to 4
heteroatoms selected from nitrogen, oxygen, and
sulphur, wherein said 5 to 6 membered heterocycle is
substituted with 0-3 R^{5c}; wherein said 5 to 6 membered
heterocycle is selected from pyridinyl, pyrimidinyl,
triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl,
piperazinyl, piperidinyl, pyrazolyl, imidazolyl,
oxazolyl, isoxazolyl, and tetrazolyl;

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R¹⁰ is H, C(=O)R¹⁷, C(=O)OR¹⁷;
C₁-C₄ alkyl optionally substituted with 0-1 R^{10a};
phenyl substituted with 0-4 R^{10b};
C₃-C₆ carbocycle substituted with 0-3 R^{10b}; or
5 to 6 membered heterocycle containing 1 to 4
heteroatoms selected from nitrogen, oxygen, and
sulphur, wherein said 5 to 6 membered heterocycle is

substituted with 0-3 R^{10b}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{10a} [, at each occurrence,] is [independently] selected from H, methyl, ethyl, propyl, butyl, OR¹⁴, Cl, F, =O, NR¹⁵R¹⁶, CF₃, or phenyl substituted with 0-4 R^{10b};

R^{10b}, at each occurrence, is independently selected from H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, Cl, F, NR¹⁵R¹⁶, and CF₃;

Z is H;

C₁-C₄ alkyl substituted with 0-3 R^{12a};

C₂-C₄ alkenyl substituted with 0-3 R^{12a}; or

C₂-C₄ alkynyl substituted with 0-3 R^{12a};

R^{12a}, at each occurrence, is independently selected from H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R¹³, at each occurrence, is independently selected from H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, Cl, F, Br, CN, NR¹⁵R¹⁶, and CF₃;

R¹⁴ is H, phenyl, benzyl, methyl, ethyl, propyl, or butyl;

R¹⁵, at each occurrence, is independently selected from H, methyl, ethyl, propyl, and butyl;

R¹⁶, at each occurrence, is independently selected from H, OH, methyl, ethyl, propyl, butyl, benzyl, phenethyl, methyl-C(=O)-, ethyl-C(=O)-, methyl-S(=O)₂-, and ethyl-S(=O)₂-;

R¹⁷ is H, methyl, ethyl, propyl, butyl, methoxymethyl, ethoxymethyl, methoxyethyl, ethoxyethyl, phenyl substituted by 0-3 R^{17a}, or -CH₂-phenyl substituted by 0-3 R^{17a};

R^{17a} is H, methyl, methoxy, -OH, F, Cl, CF₃, or OCF₃;

R¹⁸, at each occurrence, is independently selected from H, methyl, ethyl, propyl, butyl, phenyl, benzyl, and phenethyl; and

R¹⁹, at each occurrence, is independently selected from H, methyl, and ethyl.

10. (Twice Amended) A compound, according to one of Claims 6, [7,] 8, or 25 [9,] wherein:

R³ is -CH₃, -CH₂CH₃, -CH₂CH₂CH₃, -CH₂CH₂CH₂CH₃, -CH(CH₃)₂, -CH(CH₃)CH₂CH₃, -CH₂CH(CH₃)₂, -CH₂CF₃, -CH₂CH₂CF₃, -CH₂CH₂CH₂CF₃, -CH=CH₂, -CH₂CH=CH₂, -CH₂C(CH₃)=CH₂, -CH₂CH₂CH=CH₂, cis-CH₂CH=CH(CH₃), trans-CH₂CH=CH(CH₃), -C≡CH, -CH₂C≡CH, -CH₂C≡C(CH₃), cyclopropyl-CH₂-, cyclobutyl-CH₂-, cyclopentyl-CH₂-, cyclohexyl-CH₂-, cyclopropyl-CH₂CH₂-, cyclobutyl-CH₂CH₂-, cyclopentyl-CH₂CH₂-, cyclohexyl-CH₂CH₂-, phenyl-CH₂-, (2-F-phenyl)CH₂-, (3-F-phenyl)CH₂-, (4-F-phenyl)CH₂-, (2-Cl-phenyl)CH₂-, (3-Cl-phenyl)CH₂-, (4-Cl-phenyl)CH₂-, (2,3-diF-phenyl)CH₂-, (2,4-diF-phenyl)CH₂-, (2,5-diF-phenyl)CH₂-, (2,6-diF-phenyl)CH₂-, (3,4-diF-phenyl)CH₂-, (3,5-diF-phenyl)CH₂-, (2,3-diCl-phenyl)CH₂-, (2,4-diCl-phenyl)CH₂-,

(2,5-diCl-phenyl)CH₂-, (2,6-diCl-phenyl)CH₂-,
(3,4-diCl-phenyl)CH₂-, (3,5-diCl-phenyl)CH₂-,
(3-F-4-Cl-phenyl)CH₂-, (3-F-5-Cl-phenyl)CH₂-,
(3-Cl-4-F-phenyl)CH₂-, phenyl-CH₂CH₂-,
(2-F-phenyl)CH₂CH₂-, (3-F-phenyl)CH₂CH₂-,
(4-F-phenyl)CH₂CH₂-, (2-Cl-phenyl)CH₂CH₂-,
(3-Cl-phenyl)CH₂CH₂-, (4-Cl-phenyl)CH₂CH₂-,
(2,3-diF-phenyl)CH₂CH₂-, (2,4-diF-phenyl)CH₂CH₂-,
(2,5-diF-phenyl)CH₂CH₂-, (2,6-diF-phenyl)CH₂CH₂-,
(3,4-diF-phenyl)CH₂CH₂-, (3,5-diF-phenyl)CH₂CH₂-,
(2,3-diCl-phenyl)CH₂CH₂-, (2,4-diCl-phenyl)CH₂CH₂-,
(2,5-diCl-phenyl)CH₂CH₂-, (2,6-diCl-phenyl)CH₂CH₂-,
(3,4-diCl-phenyl)CH₂CH₂-, (3,5-diCl-phenyl)CH₂CH₂-,
(3-F-4-Cl-phenyl)CH₂CH₂-, or (3-F-5-Cl-phenyl)CH₂CH₂-,

R⁵ is -CH₃, -CH₂CH₃, -CH₂CH₂CH₃, -CH(CH₃)₂, -CH₂CH₂CH₂CH₃,
-CH(CH₃)CH₂CH₃, -CH₂CH(CH₃)₂, -CH₂C(CH₃)₃,
-CH₂CH₂CH₂CH₂CH₃, -CH(CH₃)CH₂CH₂CH₃, -CH₂CH(CH₃)CH₂CH₃,
-CH₂CH₂CH(CH₃)₂, -CH(CH₂CH₃)₂, -CH₂CF₃, -CH₂CH₂CF₃,
-CH₂CH₂CH₂CF₃, -CH₂CH₂CH₂CH₂CF₃, -CH=CH₂, -CH₂CH=CH₂,
-CH=CHCH₃, cis-CH₂CH=CH(CH₃), trans-CH₂CH=CH(CH₃),
trans-CH₂CH=CH(C₆H₅), -CH₂CH=C(CH₃)₂, cis-CH₂CH=CHCH₂CH₃,
trans-CH₂CH=CHCH₂CH₃, cis-CH₂CH₂CH=CH(CH₃),
trans-CH₂CH₂CH=CH(CH₃), trans-CH₂CH=CHCH₂(C₆H₅),
-C≡CH, -CH₂C≡CH, -CH₂C≡C(CH₃), -CH₂C≡C(C₆H₅),
-CH₂CH₂C≡CH, -CH₂CH₂C≡C(CH₃), -CH₂CH₂C≡C(C₆H₅),
cyclopropyl-CH₂-, cyclobutyl-CH₂-, cyclopentyl-CH₂-,
cyclohexyl-CH₂-, (2-CH₃-cyclopropyl)CH₂-,
(3-CH₃-cyclobutyl)CH₂-,
cyclopropyl-CH₂CH₂-, cyclobutyl-CH₂CH₂-,
cyclopentyl-CH₂CH₂-, cyclohexyl-CH₂CH₂-,
(2-CH₃-cyclopropyl)CH₂CH₂-, (3-CH₃-cyclobutyl)CH₂CH₂-,
phenyl-CH₂-, (2-F-phenyl)CH₂-, (3-F-phenyl)CH₂-,
(4-F-phenyl)CH₂-, furanyl-CH₂-, thienyl-CH₂-,
pyridyl-CH₂-, 1-imidazolyl-CH₂-, oxazolyl-CH₂-,
isoxazolyl-CH₂-,
phenyl-CH₂CH₂-, (2-F-phenyl)CH₂CH₂-, (3-F-phenyl)CH₂CH₂-,

(4-F-phenyl)CH₂CH₂-, furanyl-CH₂CH₂-, thienyl-CH₂CH₂-,
pyridyl-CH₂CH₂-, 1-imidazolyl-CH₂CH₂-, oxazolyl-CH₂CH₂-,
isoxazolyl-CH₂CH₂-;

Z is methyl, ethyl, i-propyl, n-propyl, n-butyl, i-butyl, s-butyl, t-butyl, or allyl;

R¹⁰ is H, methyl, ethyl, phenyl, benzyl, phenethyl,
4-F-phenyl, (4-F-phenyl)CH₂-, (4-F-phenyl)CH₂CH₂-,
4-Cl-phenyl, (4-Cl-phenyl)CH₂-, (4-Cl-phenyl)CH₂CH₂-,
4-CH₃-phenyl, (4-CH₃-phenyl)CH₂-, (4-CH₃-phenyl)CH₂CH₂-,
4-CF₃-phenyl, (4-CF₃-phenyl)CH₂-, or
(4-CF₃-phenyl)CH₂CH₂-;

R¹¹, at each occurrence, is independently selected from
H, =O, methyl, ethyl, phenyl, benzyl, phenethyl,
4-F-phenyl, (4-F-phenyl)CH₂-, (4-F-phenyl)CH₂CH₂-,
3-F-phenyl, (3-F-phenyl)CH₂-, (3-F-phenyl)CH₂CH₂-,
2-F-phenyl, (2-F-phenyl)CH₂-, (2-F-phenyl)CH₂CH₂-,
4-Cl-phenyl, (4-Cl-phenyl)CH₂-, (4-Cl-phenyl)CH₂CH₂-,
3-Cl-phenyl, (3-Cl-phenyl)CH₂-, (3-Cl-phenyl)CH₂CH₂-,
4-CH₃-phenyl, (4-CH₃-phenyl)CH₂-, (4-CH₃-phenyl)CH₂CH₂-,
3-CH₃-phenyl, (3-CH₃-phenyl)CH₂-, (3-CH₃-phenyl)CH₂CH₂-,
4-CF₃-phenyl, (4-CF₃-phenyl)CH₂-, (4-CF₃-phenyl)CH₂CH₂-,
pyrid-2-yl, pyrid-3-yl, or pyrid-4-yl, and

R¹³, at each occurrence, is independently selected from
H, F, Cl, OH, -CH₃, -CH₂CH₃, -OCH₃, or -CF₃.

11. (Amended) A compound according to Claim 2 selected from:

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-propyl-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(3R)-1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(3R)-1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-propyl-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-propyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-methyl-3-allyl-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-methyl-3-allyl-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-methyl-3-propyl-butanediamide;

(2R) N1-[1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-methyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-phenyl-7-chloro-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-phenyl-7-chloro-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(3R)-1,3-dihydro-1-methyl-2-oxo-5-phenyl-7-chloro-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-(2-fluorophenyl)-7-chloro-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-(2-fluorophenyl)-7-chloro-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(3R)-1,3-dihydro-1-methyl-2-oxo-5-(2-fluorophenyl)-7-chloro-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2S,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-phenyl-7-chloro-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-propyl-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-(2-fluorophenyl)-7-chloro-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-propyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-(4-fluorophenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-(4-fluorophenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

Amendment & Response – Docket No. DM-7076-A
Serial No.: 09/505,788
Date: April 10, 2002

(2R,3S) N1-[(3R)-1,3-dihydro-1-methyl-2-oxo-5-(4-fluorophenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-(pyrid-2-yl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-(N-morpholino)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-(dimethylamino)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-(N-methyl-N-phenylamino)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-(N-piperidinyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-(N-homopiperidinyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-(3-methoxyphenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-(pyrid-4-yl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-phenyl-7-methoxy-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-(pyrid-3-yl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-(cyclopropylmethyl)-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-(3-fluorophenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-(3-fluorophenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(3R)-1,3-dihydro-1-methyl-2-oxo-5-(3-fluorophenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-(3-buten-1-yl)-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-(cyclopentylethyl)-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-(4-trifluoromethylphenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-(3-buten-1-yl)-butanediamide;

(2R,3S) N1-[(3R)-1,3-dihydro-1-methyl-2-oxo-5-(4-trifluoromethylphenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-(3-buten-1-yl)-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-(4-trifluoromethylphenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-(4-trifluoromethylphenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(3R)-1,3-dihydro-1-methyl-2-oxo-5-(4-trifluoromethylphenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-(4-trifluoromethylphenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-n-butyl-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-(4-trifluoromethylphenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-propyl-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-(4-chlorophenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-(3-buten-1-yl)-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-(4-chlorophenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-n-butyl-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-N4-[benzyl]-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-methyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-n-butyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-(2-methylpropyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-(4-chlorophenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-ethyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-propyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

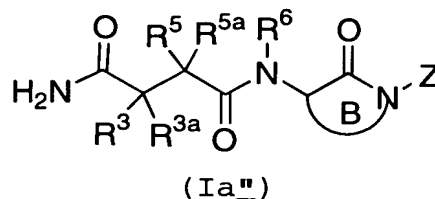
(2R,3S) N1-[1,3-dihydro-1-(isopropyl)-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3,3-diallyl-butanediamide;

[(2R,3S) N1-[6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;] and

(2R,3S) N1-[1,3,4,5-tetrahydro-1,5-dimethyl-2,4-dioxo-2H-1,5-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide.

12. (Amended) A compound, according to Claim 1, of Formula (Ia_u):



or a pharmaceutically acceptable salt thereof,
 wherein:

Z is C₁-C₈ alkyl substituted with 1-3 R¹²;
 C₂-C₄ alkenyl substituted with 1-3 R¹²;
 C₂-C₄ alkynyl substituted with 1-3 R¹²;
 C₆-C₁₀ aryl substituted with 0-4 R^{12b};
 C₃-C₁₀ carbocycle substituted with 0-4 R^{12b}; or
 5 to 10 membered heterocycle containing 1 to 4
 heteroatoms selected from nitrogen, oxygen, and
 sulfur, wherein said 5 to 10 membered heterocycle is
 substituted with 0-3 R^{12b};

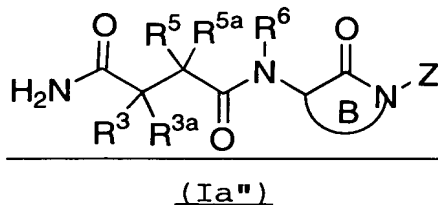
provided, when R¹³ is H,
 then Z is C₄-C₈ alkyl substituted with 1-3 R¹²;
 C₂-C₄ alkenyl substituted with 1-3 R¹²; or
 C₂-C₄ alkynyl substituted with 1-3 R¹²; and

provided, when ring B is a 1,3,4,5-tetrahydro-1-(Z)-5-(R¹⁰)-
 6,6,7,7-tetra(R¹¹)-2,4-dioxo-2H-1,5-diazepin-3-yl core, and
 R¹³ is H; then

R¹⁰ is H, C(=O)R¹⁷, C(=O)OR¹⁷, C(=O)NR¹⁸R¹⁹,
 S(=O)₂NR¹⁸R¹⁹, S(=O)₂R¹⁷; or
 C₁-C₆ alkyl optionally substituted with 0-3 R^{10a}; and

R^{10a}, at each occurrence, is independently selected from
 H, C₁-C₆ alkyl, OR¹⁴, Cl, F, Br, I, =O, CN, NO₂, NR¹⁵R¹⁶,
 and CF₃.

13. (Amended) A compound according to Claim 12 of Formula
 (Ia")



or a pharmaceutically acceptable salt thereof,
 wherein:

R³ is -(CR⁷R^{7a})_n-R⁴,
 -(CR⁷R^{7a})_n-S-(CR⁷R^{7a})_m-R⁴,
 -(CR⁷R^{7a})_n-O-(CR⁷R^{7a})_m-R⁴, or
 -(CR⁷R^{7a})_n-N(R^{7b})-(CR⁷R^{7a})_m-R⁴;

n is 0, 1, or 2;

m is 0, 1, or 2;

R^{3a} is H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy,
 propoxy, butoxy, allyl, or 3-buten-1-yl;

R⁴ is H, OH, OR^{14a},
 C₁-C₆ alkyl substituted with 0-3 R^{4a},
 C₂-C₆ alkenyl substituted with 0-3 R^{4a},
 C₂-C₆ alkynyl substituted with 0-3 R^{4a},
 C₃-C₁₀ carbocycle substituted with 0-3 R^{4b},
 C₆-C₁₀ aryl substituted with 0-3 R^{4b}, or
 5 to 10 membered heterocycle containing 1 to 4
 heteroatoms selected from nitrogen, oxygen, and
 sulphur, wherein said 5 to 10 membered heterocycle is
 substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from[is]
 H, F, Cl, Br, I, CF₃,

C₃-C₁₀ carbocycle substituted with 0-3 R^{4b},
C₆-C₁₀ aryl substituted with 0-3 R^{4b}, or
5 to 10 membered heterocycle containing 1 to 4
heteroatoms selected from nitrogen, oxygen, and
sulphur, wherein said 5 to 10 membered heterocycle is
substituted with 0-3 R^{4b};

R^{4b}, at each occurrence, is independently selected from H, OH,
Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃,
S(=O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄
haloalkyl, and C₁-C₄ haloalkoxy;

R⁵ is H, OR¹⁴;

C₁-C₆ alkyl substituted with 0-3 R^{5b};
C₁-C₆ alkoxy substituted with 0-3 R^{5b};
C₂-C₆ alkenyl substituted with 0-3 R^{5b};
C₂-C₆ alkynyl substituted with 0-3 R^{5b};
C₃-C₁₀ carbocycle substituted with 0-3 R^{5c};
C₆-C₁₀ aryl substituted with 0-3 R^{5c}; or
5 to 10 membered heterocycle containing 1 to 4
heteroatoms selected from nitrogen, oxygen, and
sulphur, wherein said 5 to 10 membered heterocycle is
substituted with 0-3 R^{5c};

R^{5a} is H or C₁-C₄ alkyl;

R^{5b}, at each occurrence, is independently selected from:
H, C₁-C₆ alkyl, CF₃, OR¹⁴, Cl, F, Br, I, =O, CN, NO₂,
NR¹⁵R¹⁶;
C₃-C₁₀ carbocycle substituted with 0-3 R^{5c};
C₆-C₁₀ aryl substituted with 0-3 R^{5c}; or
5 to 10 membered heterocycle containing 1 to 4
heteroatoms selected from nitrogen, oxygen, and
sulphur, wherein said 5 to 10 membered heterocycle is
substituted with 0-3 R^{5c};

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

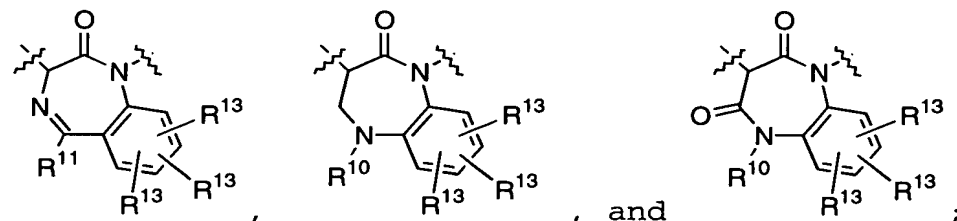
R⁶ is H, methyl, or ethyl;

R⁷, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, CF₃, phenyl, and C₁-C₄ alkyl;

R^{7a}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, CF₃, and C₁-C₄ alkyl;

R^{7b} is independently selected from H, methyl, ethyl, propyl, and butyl;

Ring B is selected from



[a 7 membered lactam or thiolactam,
wherein the lactam or thiolactam is saturated, partially
saturated or unsaturated;
wherein each additional lactam carbon or thiolactam
carbon is substituted with 0-2 R¹¹; and,
optionally, the lactam or thiolactam contains a
heteroatom selected from, -O-, -S-, -S(=O)-, -S(=O)₂-,
-N=, -NH-, and -N(R¹⁰)-;

additionally, two R¹¹ substituents on adjacent atoms may be
combined to form a benzo fused radical; wherein said
benzo fused radical is substituted with 0-3 R¹³;

additionally, two R¹¹ substituents on adjacent atoms may be combined to form a 5 to 6 membered heteroaryl fused radical, wherein said 5 to 6 membered heteroaryl fused radical comprises 1 or 2 heteroatoms selected from N, O, and S; wherein said 5 to 6 membered heteroaryl fused radical is substituted with 0-3 R¹³;

additionally, two R¹¹ substituents on the same or adjacent carbon atoms may be combined to form a C₃-C₆ carbocycle substituted with 0-3 R¹³;

R¹⁰ is H, C(=O)R¹⁷, C(=O)OR¹⁷, C(=O)NR¹⁸R¹⁹, S(=O)₂NR¹⁸R¹⁹, S(=O)₂R¹⁷;

C₁-C₆ alkyl optionally substituted with 0-2 R^{10a};

C₆-C₁₀ aryl substituted with 0-4 R^{10b};

C₃-C₁₀ carbocycle substituted with 0-3 R^{10b}; or

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{10b};

R^{10a}, at each occurrence, is independently selected from H, C₁-C₆ alkyl, OR¹⁴, Cl, F, Br, I, =O, CN, NO₂, NR¹⁵R¹⁶, CF₃, or phenyl substituted with 0-4 R^{10b};

R^{10b}, at each occurrence, is independently selected from H, OH, C₁-C₆ alkyl, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, or CF₃;

R¹¹, at each occurrence, is independently selected from H, C₁-C₄ alkoxy, Cl, F, Br, I, [=O,] CN, NO₂, NR¹⁸R¹⁹, C(=O)R¹⁷, C(=O)OR¹⁷, C(=O)NR¹⁸R¹⁹, S(=O)₂NR¹⁸R¹⁹, CF₃;
C₁-C₆ alkyl optionally substituted with 0-3 R^{11a};
C₆-C₁₀ aryl substituted with 0-3 R^{11b};
C₃-C₁₀ carbocycle substituted with 0-3 R^{11b}; or

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{11b};

R^{11a}, at each occurrence, is independently selected from H, C₁-C₆ alkyl, OR¹⁴, Cl, F, Br, I, =O, CN, NO₂, NR¹⁵R¹⁶, CF₃, or phenyl substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

Z is C₁-C₆ alkyl substituted with 1-3 R¹²;
C₂-C₄ alkenyl substituted with 1-3 R¹²;
C₂-C₄ alkynyl substituted with 1-3 R¹²;
C₆-C₁₀ aryl substituted with 0-4 R^{12b};
C₃-C₁₀ carbocycle substituted with 0-4 R^{12b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R¹², at each occurrence, is independently selected from C₆-C₁₀ aryl substituted with 0-4 R^{12b};
C₃-C₁₀ carbocycle substituted with 0-4 R^{12b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{12b}, at each occurrence, is independently selected from
H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

R¹³, at each occurrence, is independently selected from
H, OH, C₁-C₆ alkyl, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO₂,
NR¹⁵R¹⁶, and CF₃;

R¹⁴ is H, phenyl, benzyl, C₁-C₆ alkyl, or C₂-C₆ alkoxyalkyl;

R^{14a} is H, phenyl, benzyl, methyl, ethyl, propyl, or butyl;

R¹⁵, at each occurrence, is independently selected from H, C₁-
C₆ alkyl, benzyl, phenethyl, (C₁-C₆ alkyl)-C(=O)-, and
(C₁-C₆ alkyl)-S(=O)₂-;

R¹⁶, at each occurrence, is independently selected from
H, OH, C₁-C₆ alkyl, benzyl, phenethyl,
(C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-;

R¹⁷ is H, C₁-C₆ alkyl, C₂-C₆ alkoxyalkyl,
aryl substituted by 0-4 R^{17a}, or
-CH₂-aryl substituted by 0-4 R^{17a};

R^{17a} is H, methyl, ethyl, propyl, butyl, methoxy, ethoxy,
propoxy, butoxy, -OH, F, Cl, Br, I, CF₃, OCF₃, SCH₃,
S(O)CH₃, SO₂CH₃, -NH₂, -N(CH₃)₂, or C₁-C₄ haloalkyl;

R¹⁸, at each occurrence, is independently selected from
H, C₁-C₆ alkyl, phenyl, benzyl, phenethyl,
(C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-; and

R¹⁹, at each occurrence, is independently selected from
H, OH, C₁-C₆ alkyl, phenyl, benzyl, phenethyl,
(C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-;

provided, when R¹³ is H,

then Z is C₄-C₆ alkyl substituted with 1-3 R¹²;

C₂-C₄ alkenyl substituted with 1-3 R¹²; or

C₂-C₄ alkynyl substituted with 1-3 R¹².

(Ia'')



wherein:

$$R^3 \text{ is } -(\text{CHR}^7)_n - R^4,$$

n is 0 or 1;

R^{3a} is H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, allyl, or 3-buten-1-yl;

R⁴ is H, OH, OR^{14a},

C₁-C₄ alkyl substituted with 0-2 R^{4a}.

C₂-C₄ alkenyl substituted with 0-2 R^{4a}.

C₂-C₄ alkynyl substituted with 0-1 R^{4a}.

C₃-C₆ carbocycle substituted with 0-3 R^{4b}.

C₆-C₁₀ aryl substituted with 0-3 R^{4b}, or

5 to 6 membered heterocycle containing 1 to 4

heteroatoms selected from nitrogen, oxygen, and

sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{4b}:

R^{4a}, at each occurrence, is independently selected from [is]

H, F, Cl, Br, I, CF₃,

C₃-C₆ carbocycle substituted with 0-3 R^{4b}.

phenyl substituted with $O=3-R^{4b}$, or

5 to 6 membered heterocycle containing 1 to 4

heteroatoms selected from nitrogen, oxygen, and

sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{4b};

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₄ alkyl, C₁-C₃ alkoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R⁵ is H, OR¹⁴;

C₁-C₄ alkyl substituted with 0-3 R^{5b};

C₂-C₄ alkenyl substituted with 0-3 R^{5b};

C₂-C₄ alkynyl substituted with 0-3 R^{5b};

R^{5a} is H, methyl, ethyl, propyl, or butyl;

R^{5b}, at each occurrence, is independently selected from:

H, methyl, ethyl, propyl, butyl, CF₃, OR¹⁴, Cl, F, Br, I, =O;

C₃-C₆ carbocycle substituted with 0-3 R^{5c};

phenyl substituted with 0-3 R^{5c}; or

5 to 6 membered heterocycle containing 1 to 4

heteroatoms selected from nitrogen, oxygen, and

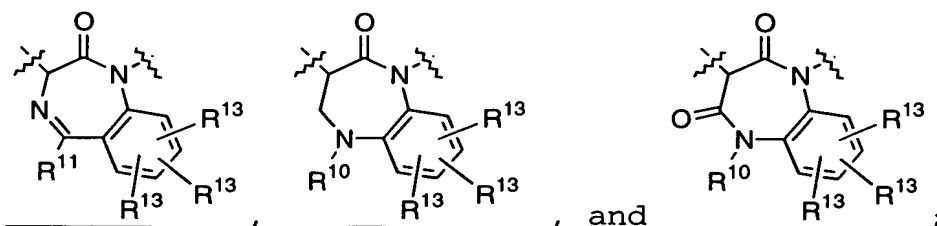
sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{5c};

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₄ alkyl, C₁-C₃ alkoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R⁶ is H;

R⁷, at each occurrence, is independently selected from H, F, CF₃, methyl, and ethyl;

Ring B is selected from



[a 7 membered lactam or thiolactam,
 wherein the lactam or thiolactam is saturated, partially saturated or
 unsaturated;

wherein each additional lactam carbon or thiolactam
 carbon is substituted with 0-2 R¹¹; and,
 optionally, the lactam or thiolactam contains a
 heteroatom selected from -N=, -NH-, and -N(R¹⁰)-;

additionally, two R¹¹ substituents on adjacent atoms may be
 combined to form a benzo fused radical; wherein said
 benzo fused radical is substituted with 0-2 R¹³;

additionally, two R¹¹ substituents on adjacent atoms may be
 combined to form a 5 to 6 membered heteroaryl fused
 radical, wherein said 5 to 6 membered heteroaryl fused
 radical comprises 1 or 2 heteroatoms selected from N, O,
 and S; wherein said 5 to 6 membered heteroaryl fused
 radical is substituted with 0-2 R¹³;

additionally, two R¹¹ substituents on the same or adjacent
 carbon atoms may be combined to form a C₃-C₆ carbocycle
 substituted with 0-2 R¹³;

R¹⁰ is H, C(=O)R¹⁷, C(=O)OR¹⁷;

C₁-C₄ alkyl optionally substituted with 0-1 R^{10a};

phenyl substituted with 0-4 R^{10b};

C₃-C₆ carbocycle substituted with 0-3 R^{10b}; or

5 to 6 membered heterocycle containing 1 to 4

heteroatoms selected from nitrogen, oxygen, and

sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{10b};

R^{10a} [, at each occurrence,] is [independently] selected from H, C₁-C₄ alkyl, OR¹⁴, Cl, F, Br, I, =O, CN, NO₂, NR¹⁵R¹⁶, CF₃, or phenyl substituted with 0-4 R^{10b};

R^{10b}, at each occurrence, is independently selected from H, OH, C₁-C₄ alkyl, C₁-C₃ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, or CF₃;

R¹¹ [, at each occurrence,] is [independently] selected from H, C₁-C₄ alkoxy, Cl, F, [=O,] NR¹⁸R¹⁹, C(=O)R¹⁷, C(=O)OR¹⁷, CF₃;
C₁-C₆ alkyl optionally substituted with 0-3 R^{11a};
C₆-C₁₀ aryl substituted with 0-3 R^{11b};
C₃-C₆ carbocycle substituted with 0-3 R^{11b}; or
5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{11b};

R^{11a}, at each occurrence, is independently selected from H, C₁-C₄ alkyl, OR¹⁴, F, =O, NR¹⁵R¹⁶, CF₃, or phenyl substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, C₁-C₄ alkyl, C₁-C₃ alkoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

Z is C₁-C₄ alkyl substituted with 1-3 R¹²;
C₂-C₄ alkenyl substituted with 1-3 R¹²;
C₂-C₄ alkynyl substituted with 1-3 R¹²;
C₆-C₁₀ aryl substituted with 0-4 R^{12b};
C₃-C₆ carbocycle substituted with 0-4 R^{12b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and

sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{12b};

R¹², at each occurrence, is independently selected from C₆-C₁₀ aryl substituted with 0-4 R^{12b}; C₃-C₆ carbocycle substituted with 0-4 R^{12b}; or 5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{12b}, at each occurrence, is independently selected from H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₄ alkyl, C₁-C₃ alkoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R¹³, at each occurrence, is independently selected from H, OH, C₁-C₆ alkyl, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, and CF₃;

R¹⁴ is H, phenyl, benzyl, C₁-C₄ alkyl, or C₂-C₄ alkoxyalkyl;

R¹⁵, at each occurrence, is independently selected from H, C₁-C₄ alkyl, benzyl, phenethyl, (C₁-C₄ alkyl)-C(=O)-, and (C₁-C₄ alkyl)-S(=O)₂-;

R¹⁶, at each occurrence, is independently selected from H, OH, C₁-C₄ alkyl, benzyl, phenethyl, (C₁-C₄ alkyl)-C(=O)-, and (C₁-C₄ alkyl)-S(=O)₂-;

R¹⁷ is H, methyl, ethyl, propyl, butyl, methoxymethyl, ethoxymethyl, methoxyethyl, ethoxyethyl, phenyl substituted by 0-3 R^{17a}, or -CH₂-phenyl substituted by 0-3 R^{17a};

R^{17a} is H, methyl, methoxy, -OH, F, Cl, CF₃, or OCF₃;

R¹⁸, at each occurrence, is independently selected from H, methyl, ethyl, propyl, butyl, phenyl, benzyl, and phenethyl; and

R¹⁹, at each occurrence, is independently selected from H, methyl, and ethyl;

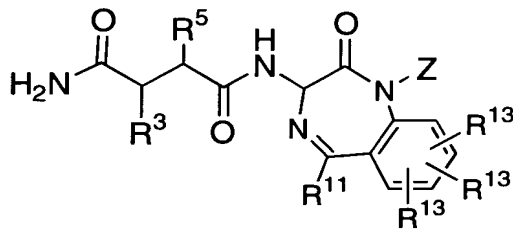
provided, when R¹³ is H,

then Z is butyl substituted with 1-3 R¹²;

C₂-C₄ alkenyl substituted with 1-3 R¹²; or

C₂-C₄ alkynyl substituted with 1-3 R¹².

16. (Twice Amended) A compound according to Claim **14** **[15]** of Formula (Ic):



(Ic)

or a pharmaceutically acceptable salt thereof
wherein

R³ is R⁴,

R⁴ is C₁-C₄ alkyl substituted with 0-1 R^{4a},

C₂-C₄ alkenyl substituted with 0-1 R^{4a}, or

C₂-C₄ alkynyl substituted with 0-1 R^{4a};

R^{4a} [, at each occurrence,] is [independently] selected from
H, F, CF₃,

C₃-C₆ carbocycle substituted with 0-3 R^{4b},

phenyl substituted with 0-3 R^{4b}, or

5 to 6 membered heterocycle containing 1 to 4

heteroatoms selected from nitrogen, oxygen, and

sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{4b}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R⁵ is C₁-C₄ alkyl substituted with 0-1 R^{5b};
C₂-C₄ alkenyl substituted with 0-1 R^{5b};
C₂-C₄ alkynyl substituted with 0-1 R^{5b};

R^{5b}[, at each occurrence,] is [independently] selected from:
H, methyl, ethyl, propyl, butyl, CF₃, OR¹⁴, =O;
C₃-C₆ carbocycle substituted with 0-2 R^{5c};
phenyl substituted with 0-3 R^{5c}; or
5 to 6 membered heterocycle containing 1 to 4
heteroatoms selected from nitrogen, oxygen, and
sulphur, wherein said 5 to 6 membered heterocycle is
substituted with 0-3 R^{5c}; wherein said 5 to 6 membered
heterocycle is selected from pyridinyl, pyrimidinyl,
triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl,
piperazinyl, piperidinyl, pyrazolyl, imidazolyl,
oxazolyl, isoxazolyl, and tetrazolyl;

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R¹¹[, at each occurrence,] is [independently] selected from
H, [=O,] NR¹⁸R¹⁹, CF₃;
C₁-C₄ alkyl optionally substituted with 0-1 R^{11a};

phenyl substituted with 0-3 R^{11b};
C₃-C₆ carbocycle substituted with 0-3 R^{11b}; or
5 to 6 membered heterocycle containing 1 to 4
heteroatoms selected from nitrogen, oxygen, and
sulphur, wherein said 5 to 6 membered heterocycle is
substituted with 0-3 R^{11b}; wherein said 5 to 6
membered heterocycle is selected from pyridinyl,
pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl,
pyrrolyl, piperazinyl, piperidinyl, pyrazolyl,
imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{11a} [, at each occurrence,] is [independently] selected from
H, C₁-C₄ alkyl, OR¹⁴, F, [Cl,] =O, NR¹⁵R¹⁶, CF₃, or
phenyl substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H,
OH, Cl, F, NR¹⁵R¹⁶, CF₃, methyl, ethyl, propyl, butyl,
methoxy, ethoxy, propoxy, C₁-C₂ haloalkyl, and C₁-C₂
haloalkoxy;

Z is C₁-C₃ alkyl substituted with 1-3 R¹²;
C₂-C₃ alkenyl substituted with 1-3 R¹²;
C₂-C₃ alkynyl substituted with 1-3 R¹²;
C₆-C₁₀ aryl substituted with 0-4 R^{12b};
C₃-C₆ carbocycle substituted with 0-3 R^{12b}; or
5 to 6 membered heterocycle containing 1 to 4
heteroatoms selected from nitrogen, oxygen, and
sulphur, wherein said 5 to 6 membered heterocycle is
substituted with 0-3 R^{12b}; wherein said 5 to 6
membered heterocycle is selected from pyridinyl,
pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl,
pyrrolyl, piperazinyl, piperidinyl, pyrazolyl,
imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R¹², at each occurrence, is independently selected from
C₆-C₁₀ aryl substituted with 0-4 R^{12b};
C₃-C₆ carbocycle substituted with 0-3 R^{12b}; or

5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{12b}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{12b}, at each occurrence, is independently selected from H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R¹³, at each occurrence, is independently selected from H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, Cl, F, Br, CN, NR¹⁵R¹⁶, and CF₃;

R¹⁴ is H, phenyl, benzyl, methyl, ethyl, propyl, or butyl;

R¹⁵, at each occurrence, is independently selected from H, methyl, ethyl, propyl, and butyl;

R¹⁶, at each occurrence, is independently selected from H, OH, methyl, ethyl, propyl, butyl, benzyl, phenethyl, methyl-C(=O)-, ethyl-C(=O)-, methyl-S(=O)₂-, and ethyl-S(=O)₂-;

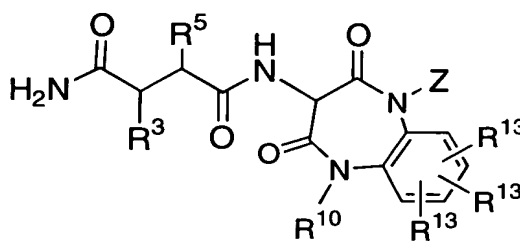
R¹⁸, at each occurrence, is independently selected from H, methyl, ethyl, propyl, butyl, phenyl, benzyl, and phenethyl; and

R¹⁹, at each occurrence, is independently selected from
H, methyl, and ethyl;

provided, when R¹³ is H,
then Z is C₂-C₃ alkenyl substituted with 1-3 R¹²; or

C₂-C₃ alkynyl substituted with 1-3 R¹².

18. (Twice Amended) A compound according to Claim 14 [15] of Formula (Ie):



(Ie)

or a pharmaceutically acceptable salt thereof wherein:

R³ is R⁴,

R⁴ is C₁-C₄ alkyl substituted with 0-1 R^{4a},
C₂-C₄ alkenyl substituted with 0-1 R^{4a}, or
C₂-C₄ alkynyl substituted with 0-1 R^{4a};

R^{4a} [, at each occurrence,] is [independently] selected from
H, F, CF₃,
C₃-C₆ carbocycle substituted with 0-3 R^{4b},
phenyl substituted with 0-3 R^{4b}, or
5 to 6 membered heterocycle containing 1 to 4
heteroatoms selected from nitrogen, oxygen, and
sulphur, wherein said 5 to 6 membered heterocycle is
substituted with 0-3 R^{4b}; wherein said 5 to 6 membered
heterocycle is selected from pyridinyl, pyrimidinyl,
triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl,
piperazinyl, piperidinyl, pyrazolyl, imidazolyl,
oxazolyl, isoxazolyl, and tetrazolyl;

R^{4b}, at each occurrence, is independently selected from H, OH,
Cl, F, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃,
methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy,
C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R⁵ is C₁-C₄ alkyl substituted with 0-1 R^{5b};
C₂-C₄ alkenyl substituted with 0-1 R^{5b};
C₂-C₄ alkynyl substituted with 0-1 R^{5b};

R^{5b} [, at each occurrence,] is [independently] selected from:
H, methyl, ethyl, propyl, butyl, CF₃, OR¹⁴, =O;
C₃-C₆ carbocycle substituted with 0-2 R^{5c};
phenyl substituted with 0-3 R^{5c}; or
5 to 6 membered heterocycle containing 1 to 4
heteroatoms selected from nitrogen, oxygen, and
sulphur, wherein said 5 to 6 membered heterocycle is
substituted with 0-3 R^{5c}; wherein said 5 to 6 membered
heterocycle is selected from pyridinyl, pyrimidinyl,
triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl,
piperazinyl, piperidinyl, pyrazolyl, imidazolyl,
oxazolyl, isoxazolyl, and tetrazolyl;

R^{5c}, at each occurrence, is independently selected from H, OH,
Cl, F, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃,
methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy,
C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R¹⁰ is H, C(=O)R¹⁷, C(=O)OR¹⁷;
C₁-C₄ alkyl optionally substituted with 0-1 R^{10a};
phenyl substituted with 0-4 R^{10b};
C₃-C₆ carbocycle substituted with 0-3 R^{10b}; or
5 to 6 membered heterocycle containing 1 to 4
heteroatoms selected from nitrogen, oxygen, and
sulphur, wherein said 5 to 6 membered heterocycle is
substituted with 0-3 R^{10b}; wherein said 5 to 6
membered heterocycle is selected from pyridinyl,
pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl,
pyrrolyl, piperazinyl, piperidinyl, pyrazolyl,
imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{10a} [, at each occurrence,] is [independently] selected from H, methyl, ethyl, propyl, butyl, OR¹⁴, Cl, F, =O, NR¹⁵R¹⁶, CF₃, or phenyl substituted with 0-4 R^{10b};

R^{10b}, at each occurrence, is independently selected from H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, Cl, F, NR¹⁵R¹⁶, and CF₃;

Z is C₁-C₃ alkyl substituted with 1-3 R¹²;
C₂-C₃ alkenyl substituted with 1-3 R¹²;
C₂-C₃ alkynyl substituted with 1-3 R¹²;
C₆-C₁₀ aryl substituted with 0-4 R^{12b};
C₃-C₆ carbocycle substituted with 0-3 R^{12b}; or
5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{12b}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R¹², at each occurrence, is independently selected from C₆-C₁₀ aryl substituted with 0-4 R^{12b};
C₃-C₆ carbocycle substituted with 0-3 R^{12b}; or
5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{12b}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{12b}, at each occurrence, is independently selected from

H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃,
S(=O)₂CH₃, methyl, ethyl, propyl, butyl, methoxy, ethoxy,
propoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R¹³, at each occurrence, is independently selected from
H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy,
Cl, F, Br, CN, NR¹⁵R¹⁶, and CF₃;

R¹⁴ is H, phenyl, benzyl, methyl, ethyl, propyl, or butyl;

R¹⁵, at each occurrence, is independently selected from H,
methyl, ethyl, propyl, and butyl;

R¹⁶, at each occurrence, is independently selected from
H, OH, methyl, ethyl, propyl, butyl, benzyl, phenethyl,
methyl-C(=O)-, ethyl-C(=O)-,
methyl-S(=O)₂-, and ethyl-S(=O)₂-;

R¹⁷ is H, methyl, ethyl, propyl, butyl, methoxymethyl,
ethoxymethyl, methoxyethyl, ethoxyethyl,
phenyl substituted by 0-3 R^{17a}, or
-CH₂-phenyl substituted by 0-3 R^{17a};

R^{17a} is H, methyl, methoxy, -OH, F, Cl, CF₃, or OCF₃;

R¹⁸, at each occurrence, is independently selected from
H, methyl, ethyl, propyl, butyl, phenyl, benzyl, and
phenethyl; and

R¹⁹, at each occurrence, is independently selected from
H, methyl, and ethyl;

~~provided, when R¹³ is H,~~
then Z is C₂-C₃ alkenyl substituted with 1-3 R¹²; or
C₂-C₃ alkynyl substituted with 1-3 R¹².

20. (Twice Amended) A compound according to one of Claims 16, [17,] 18, or 26 [19,] wherein:

R³ is -CH₃, -CH₂CH₃, -CH₂CH₂CH₃, -CH₂CH₂CH₂CH₃,
-CH(CH₃)₂, -CH(CH₃)CH₂CH₃, -CH₂CH(CH₃)₂,
-CH₂CF₃, -CH₂CH₂CF₃, -CH₂CH₂CH₂CF₃,
-CH=CH₂, -CH₂CH=CH₂, -CH₂C(CH₃)=CH₂,
-CH₂CH₂CH=CH₂,
cis-CH₂CH=CH(CH₃),
trans-CH₂CH=CH(CH₃),
-C≡CH, -CH₂C≡CH, -CH₂C≡C(CH₃),
cyclopropyl-CH₂-, cyclobutyl-CH₂-, cyclopentyl-CH₂-,
cyclohexyl-CH₂-, cyclopropyl-CH₂CH₂-,
cyclobutyl-CH₂CH₂-, cyclopentyl-CH₂CH₂-,
cyclohexyl-CH₂CH₂-, phenyl-CH₂-,
(2-F-phenyl)CH₂-, (3-F-phenyl)CH₂-, (4-F-phenyl)CH₂-,
(2-Cl-phenyl)CH₂-, (3-Cl-phenyl)CH₂-, (4-Cl-phenyl)CH₂-,
(2,3-diF-phenyl)CH₂-, (2,4-diF-phenyl)CH₂-,
(2,5-diF-phenyl)CH₂-, (2,6-diF-phenyl)CH₂-,
(3,4-diF-phenyl)CH₂-, (3,5-diF-phenyl)CH₂-,
(2,3-diCl-phenyl)CH₂-, (2,4-diCl-phenyl)CH₂-,
(2,5-diCl-phenyl)CH₂-, (2,6-diCl-phenyl)CH₂-,
(3,4-diCl-phenyl)CH₂-, (3,5-diCl-phenyl)CH₂-,
(3-F-4-Cl-phenyl)CH₂-, (3-F-5-Cl-phenyl)CH₂-,
(3-Cl-4-F-phenyl)CH₂-, phenyl-CH₂CH₂-,
(2-F-phenyl)CH₂CH₂-, (3-F-phenyl)CH₂CH₂-,
(4-F-phenyl)CH₂CH₂-, (2-Cl-phenyl)CH₂CH₂-,
(3-Cl-phenyl)CH₂CH₂-, (4-Cl-phenyl)CH₂CH₂-,
(2,3-diF-phenyl)CH₂CH₂-, (2,4-diF-phenyl)CH₂CH₂-,
(2,5-diF-phenyl)CH₂CH₂-, (2,6-diF-phenyl)CH₂CH₂-,
(3,4-diF-phenyl)CH₂CH₂-, (3,5-diF-phenyl)CH₂CH₂-,
(2,3-diCl-phenyl)CH₂CH₂-, (2,4-diCl-phenyl)CH₂CH₂-,
(2,5-diCl-phenyl)CH₂CH₂-, (2,6-diCl-phenyl)CH₂CH₂-,
(3,4-diCl-phenyl)CH₂CH₂-, (3,5-diCl-phenyl)CH₂CH₂-,
(3-F-4-Cl-phenyl)CH₂CH₂-, or (3-F-5-Cl-phenyl)CH₂CH₂-,

R⁵ is -CH₃, -CH₂CH₃, -CH₂CH₂CH₃, -CH(CH₃)₂, -CH₂CH₂CH₂CH₃,

-CH(CH₃)CH₂CH₃, -CH₂CH(CH₃)₂, -CH₂C(CH₃)₃,
-CH₂CH₂CH₂CH₂CH₃, -CH(CH₃)CH₂CH₂CH₃, -CH₂CH(CH₃)CH₂CH₃,
-CH₂CH₂CH(CH₃)₂, -CH(CH₂CH₃)₂, -CH₂CF₃, -CH₂CH₂CF₃,
-CH₂CH₂CH₂CF₃, -CH₂CH₂CH₂CH₂CF₃, -CH=CH₂, -CH₂CH=CH₂,
-CH=CHCH₃, cis-CH₂CH=CH(CH₃), trans-CH₂CH=CH(CH₃),
trans-CH₂CH=CH(C₆H₅), -CH₂CH=C(CH₃)₂, cis-CH₂CH=CHCH₂CH₃,
trans-CH₂CH=CHCH₂CH₃, cis-CH₂CH₂CH=CH(CH₃),
trans-CH₂CH₂CH=CH(CH₃), trans-CH₂CH=CHCH₂(C₆H₅),
-C≡CH, -CH₂C≡CH, -CH₂C≡C(CH₃), -CH₂C≡C(C₆H₅),
-CH₂CH₂C≡CH, -CH₂CH₂C≡C(CH₃), -CH₂CH₂C≡C(C₆H₅),
cyclopropyl-CH₂-, cyclobutyl-CH₂-, cyclopentyl-CH₂-,
cyclohexyl-CH₂-, (2-CH₃-cyclopropyl)CH₂-,
(3-CH₃-cyclobutyl)CH₂-,
cyclopropyl-CH₂CH₂-, cyclobutyl-CH₂CH₂-,
cyclopentyl-CH₂CH₂-, cyclohexyl-CH₂CH₂-,
(2-CH₃-cyclopropyl)CH₂CH₂-, (3-CH₃-cyclobutyl)CH₂CH₂-,
phenyl-CH₂-, (2-F-phenyl)CH₂-, (3-F-phenyl)CH₂-,
(4-F-phenyl)CH₂-, furanyl-CH₂-, thienyl-CH₂-,
pyridyl-CH₂-, 1-imidazolyl-CH₂-, oxazolyl-CH₂-,
isoxazolyl-CH₂-,
phenyl-CH₂CH₂-, (2-F-phenyl)CH₂CH₂-, (3-F-phenyl)CH₂CH₂-,
(4-F-phenyl)CH₂CH₂-, furanyl-CH₂CH₂-, thienyl-CH₂CH₂-,
pyridyl-CH₂CH₂-, 1-imidazolyl-CH₂CH₂-, oxazolyl-CH₂CH₂-,
isoxazolyl-CH₂CH₂-;

Z is phenyl, 2-F-phenyl, 3-F-phenyl, 4-F-phenyl,
2-Cl-phenyl, 3-Cl-phenyl, 4-Cl-phenyl, 2,3-diF-phenyl,
2,4-diF-phenyl, 2,5-diF-phenyl, 2,6-diF-phenyl,
3,4-diF-phenyl, 3,5-diF-phenyl, 2,3-diCl-phenyl,
2,4-diCl-phenyl, 2,5-diCl-phenyl, 2,6-diCl-phenyl,
3,4-diCl-phenyl, 3,5-diCl-phenyl, 3-F-4-Cl-phenyl,
3-F-5-Cl-phenyl, 3-Cl-4-F-phenyl, 2-MeO-phenyl,
3-MeO-phenyl, 4-MeO-phenyl, 2-Me-phenyl, 3-Me-phenyl,
4-Me-phenyl, 2-MeS-phenyl, 3-MeS-phenyl, 4-MeS-phenyl,
2-CF₃O-phenyl, 3-CF₃O-phenyl, 4-CF₃O-phenyl,
furanyl, thienyl, pyridyl, 2-Me-pyridyl, 3-Me-pyridyl,
4-Me-pyridyl, 1-imidazolyl, oxazolyl, isoxazolyl,

cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl,
N-piperidinyl,
phenyl-CH₂-, (2-F-phenyl)CH₂-, (3-F-phenyl)CH₂-,
(4-F-phenyl)CH₂-, (2-Cl-phenyl)CH₂-, (3-Cl-phenyl)CH₂-, (4-
Cl-phenyl)CH₂-, (2,3-diF-phenyl)CH₂-,
(2,4-diF-phenyl)CH₂-, (2,5-diF-phenyl)CH₂-,
(2,6-diF-phenyl)CH₂-, (3,4-diF-phenyl)CH₂-,
(3,5-diF-phenyl)CH₂-, (2,3-diCl-phenyl)CH₂-,
(2,4-diCl-phenyl)CH₂-, (2,5-diCl-phenyl)CH₂-,
(2,6-diCl-phenyl)CH₂-, (3,4-diCl-phenyl)CH₂-,
(3,5-diCl-phenyl)CH₂-, (3-F-4-Cl-phenyl)CH₂-,
(3-F-5-Cl-phenyl)CH₂-, (3-Cl-4-F-phenyl)CH₂-,
(2-MeO-phenyl)CH₂-, (3-MeO-phenyl)CH₂-,
(4-MeO-phenyl)CH₂-, (2-Me-phenyl)CH₂-,
(3-Me-phenyl)CH₂-, (4-Me-phenyl)CH₂-,
(2-MeS-phenyl)CH₂-, (3-MeS-phenyl)CH₂-,
4-MeS-phenyl)CH₂-, (2-CF₃O-phenyl)CH₂-,
(3-CF₃O-phenyl)CH₂-, (4-CF₃O-phenyl)CH₂-,
(furanyl)CH₂-, (thienyl)CH₂-, (pyridyl)CH₂-,
(2-Me-pyridyl)CH₂-, (3-Me-pyridyl)CH₂-,
(4-Me-pyridyl)CH₂-, (1-imidazolyl)CH₂-,
(oxazolyl)CH₂-, (isoxazolyl)CH₂-,
(cyclopropyl)CH₂-, (cyclobutyl)CH₂-, (cyclopentyl)CH₂-,
(cyclohexyl)CH₂-, (N-piperidinyl)CH₂-,

phenyl-CH₂CH₂-, (phenyl)₂CHCH₂-, (2-F-phenyl)CH₂CH₂-,
(3-F-phenyl)CH₂CH₂-, (4-F-phenyl)CH₂CH₂-,
(2-Cl-phenyl)CH₂CH₂-, (3-Cl-phenyl)CH₂CH₂-,
(4-Cl-phenyl)CH₂CH₂-, (2,3-diF-phenyl)CH₂CH₂-,
(2,4-diF-phenyl)CH₂CH₂-, (2,5-diF-phenyl)CH₂CH₂-,
(2,6-diF-phenyl)CH₂CH₂-, (3,4-diF-phenyl)CH₂CH₂-,
(3,5-diF-phenyl)CH₂CH₂-, (2,3-diCl-phenyl)CH₂CH₂-,
(2,4-diCl-phenyl)CH₂CH₂-, (2,5-diCl-phenyl)CH₂CH₂-,
(2,6-diCl-phenyl)CH₂CH₂-, (3,4-diCl-phenyl)CH₂CH₂-,
(3,5-diCl-phenyl)CH₂CH₂-, (3-F-4-Cl-phenyl)CH₂CH₂-,
(3-F-5-Cl-phenyl)CH₂CH₂-, (3-Cl-4-F-phenyl)CH₂CH₂-,
(2-MeO-phenyl)CH₂CH₂-, (3-MeO-phenyl)CH₂CH₂-,

(4-MeO-phenyl)CH₂CH₂-, (2-Me-phenyl)CH₂CH₂-,
(3-Me-phenyl)CH₂CH₂-, (4-Me-phenyl)CH₂CH₂-,
(2-MeS-phenyl)CH₂CH₂-, (3-MeS-phenyl)CH₂CH₂-,
(4-MeS-phenyl)CH₂CH₂-, (2-CF₃O-phenyl)CH₂CH₂-,
(3-CF₃O-phenyl)CH₂CH₂-, (4-CF₃O-phenyl)CH₂CH₂-,
(furanyl)CH₂CH₂-, (thienyl)CH₂CH₂-, (pyridyl)CH₂CH₂-,
(2-Me-pyridyl)CH₂CH₂-, (3-Me-pyridyl)CH₂CH₂-,
(4-Me-pyridyl)CH₂CH₂-, (imidazolyl)CH₂CH₂-,
(oxazolyl)CH₂CH₂-, (isoxazolyl)CH₂CH₂-,
(cyclopropyl)CH₂CH₂-, (cyclobutyl)CH₂CH₂-,
(cyclopentyl)CH₂CH₂-, (cyclohexyl)CH₂CH₂-, or
(N-piperidinyl)CH₂CH₂-;

R¹⁰ is H, methyl, ethyl, phenyl, benzyl, phenethyl,
4-F-phenyl, (4-F-phenyl)CH₂-, (4-F-phenyl)CH₂CH₂-,
4-Cl-phenyl, (4-Cl-phenyl)CH₂-, (4-Cl-phenyl)CH₂CH₂-,
4-CH₃-phenyl, (4-CH₃-phenyl)CH₂-, (4-CH₃-phenyl)CH₂CH₂-,
4-CF₃-phenyl, (4-CF₃-phenyl)CH₂-, or
(4-CF₃-phenyl)CH₂CH₂-;

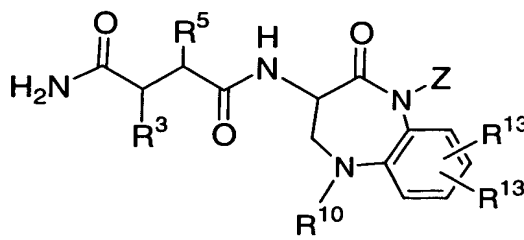
R¹¹, at each occurrence, is independently selected from
H, =O, methyl, ethyl, phenyl, benzyl, phenethyl,
4-F-phenyl, (4-F-phenyl)CH₂-, (4-F-phenyl)CH₂CH₂-,
3-F-phenyl, (3-F-phenyl)CH₂-, (3-F-phenyl)CH₂CH₂-,
2-F-phenyl, (2-F-phenyl)CH₂-, (2-F-phenyl)CH₂CH₂-,
4-Cl-phenyl, (4-Cl-phenyl)CH₂-, (4-Cl-phenyl)CH₂CH₂-,
3-Cl-phenyl, (3-Cl-phenyl)CH₂-, (3-Cl-phenyl)CH₂CH₂-,
4-CH₃-phenyl, (4-CH₃-phenyl)CH₂-, (4-CH₃-phenyl)CH₂CH₂-,
3-CH₃-phenyl, (3-CH₃-phenyl)CH₂-, (3-CH₃-phenyl)CH₂CH₂-,
4-CF₃-phenyl, (4-CF₃-phenyl)CH₂-, (4-CF₃-phenyl)CH₂CH₂-,
pyrid-2-yl, pyrid-3-yl, or pyrid-4-yl, and

R¹³, at each occurrence, is independently selected from
H, F, Cl, OH, -CH₃, -CH₂CH₃, -OCH₃, or -CF₃.

22. A pharmaceutical composition comprising a compound of Claim 1 and a pharmaceutically acceptable carrier.

23. (Amended) A method for the treatment of Alzheimer's Disease [neurological disorders associated with β -amyloid] production comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of Claim 1.

25. (New) A compound according to Claim 4 of Formula (Iq):



(Iq)

or a pharmaceutically acceptable salt thereof wherein:

$$\mathbb{R}^3 \text{ is } \mathbb{R}^4,$$

R⁴ is C₁-C₄ alkyl substituted with 0-1 R^{4a},
C₂-C₄ alkenyl substituted with 0-1 R^{4a}, or
C₂-C₄ alkynyl substituted with 0-1 R^{4a};

R^{4a}, at each occurrence, is independently selected from

H, F, CF₃,

C₃-C₆ carbocycle substituted with 0-3 R^{4b}.

phenyl substituted with 0-3 R^{4b}, or

5 to 6 membered heterocycle containing 1 to 4

heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{4b}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl,

piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R⁵ is C₁-C₄ alkyl substituted with 0-1 R^{5b};
C₂-C₄ alkenyl substituted with 0-1 R^{5b};
C₂-C₄ alkynyl substituted with 0-1 R^{5b};

R^{5b} is selected from:

H, methyl, ethyl, propyl, butyl, CF₃, OR¹⁴, =O;
C₃-C₆ carbocycle substituted with 0-2 R^{5c};
phenyl substituted with 0-3 R^{5c}; or
5 to 6 membered heterocycle containing 1 to 4
heteroatoms selected from nitrogen, oxygen, and
sulphur, wherein said 5 to 6 membered heterocycle is
substituted with 0-3 R^{5c}; wherein said 5 to 6 membered
heterocycle is selected from pyridinyl, pyrimidinyl,
triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl,
piperazinyl, piperidinyl, pyrazolyl, imidazolyl,
oxazolyl, isoxazolyl, and tetrazolyl;

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R¹⁰ is H, C(=O)R¹⁷, C(=O)OR¹⁷;

C₁-C₄ alkyl optionally substituted with 0-1 R^{10a};

phenyl substituted with 0-4 R^{10b};

C₃-C₆ carbocycle substituted with 0-3 R^{10b}; or

5 to 6 membered heterocycle containing 1 to 4

heteroatoms selected from nitrogen, oxygen, and
sulphur, wherein said 5 to 6 membered heterocycle is

substituted with 0-3 R^{10b}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{10a} is selected from H, methyl, ethyl, propyl, butyl, OR¹⁴, Cl, F, =O, NR¹⁵R¹⁶, CF₃, or phenyl substituted with 0-4 R^{10b};

R^{10b}, at each occurrence, is independently selected from H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, Cl, F, NR¹⁵R¹⁶, and CF₃;

Z is H;

C₁-C₄ alkyl substituted with 0-3 R^{12a};

C₂-C₄ alkenyl substituted with 0-3 R^{12a}; or

C₂-C₄ alkynyl substituted with 0-3 R^{12a};

R^{12a}, at each occurrence, is independently selected from H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R¹³, at each occurrence, is independently selected from H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, Cl, F, Br, CN, NR¹⁵R¹⁶, and CF₃;

R¹⁴ is H, phenyl, benzyl, methyl, ethyl, propyl, or butyl;

R¹⁵, at each occurrence, is independently selected from H, methyl, ethyl, propyl, and butyl;

R¹⁶, at each occurrence, is independently selected from H, OH, methyl, ethyl, propyl, butyl, benzyl, phenethyl, methyl-C(=O)-, ethyl-C(=O)-, methyl-S(=O)₂-, and ethyl-S(=O)₂-;

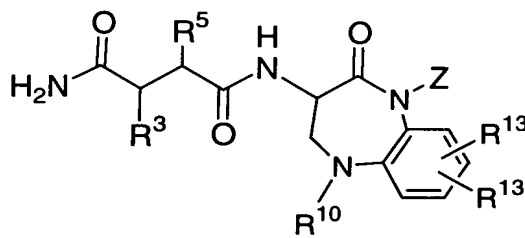
R¹⁷ is H, methyl, ethyl, propyl, butyl, methoxymethyl, ethoxymethyl, methoxyethyl, ethoxyethyl, phenyl substituted by 0-3 R^{17a}, or -CH₂-phenyl substituted by 0-3 R^{17a};

R^{17a} is H, methyl, methoxy, -OH, F, Cl, CF₃, or OCF₃;

R¹⁸, at each occurrence, is independently selected from H, methyl, ethyl, propyl, butyl, phenyl, benzyl, and phenethyl; and

R¹⁹, at each occurrence, is independently selected from H, methyl, and ethyl.

26. (New) A compound according to Claim 14 of Formula (Iq):



(Iq)

or a pharmaceutically acceptable salt thereof wherein:

R³ is R⁴,

R⁴ is C₁-C₄ alkyl substituted with 0-1 R^{4a},
C₂-C₄ alkenyl substituted with 0-1 R^{4a}, or
C₂-C₄ alkynyl substituted with 0-1 R^{4a};

R^{4a} is selected from

H, F, CF₃,

C₃-C₆ carbocycle substituted with 0-3 R^{4b},

phenyl substituted with 0-3 R^{4b}, or

5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{4b}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R⁵ is C₁-C₄ alkyl substituted with 0-1 R^{5b};
C₂-C₄ alkenyl substituted with 0-1 R^{5b};
C₂-C₄ alkynyl substituted with 0-1 R^{5b};

R^{5b} is selected from:

H, methyl, ethyl, propyl, butyl, CF₃, OR¹⁴, =O;
C₃-C₆ carbocycle substituted with 0-2 R^{5c};
phenyl substituted with 0-3 R^{5c}; or
5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{5c}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R¹⁰ is H, C(=O)R¹⁷, C(=O)OR¹⁷;

C₁-C₄ alkyl optionally substituted with 0-1 R^{10a};
phenyl substituted with 0-4 R^{10b};
C₃-C₆ carbocycle substituted with 0-3 R^{10b}; or
5 to 6 membered heterocycle containing 1 to 4
heteroatoms selected from nitrogen, oxygen, and
sulphur, wherein said 5 to 6 membered heterocycle is
substituted with 0-3 R^{10b}; wherein said 5 to 6
membered heterocycle is selected from pyridinyl,
pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl,
pyrrolyl, piperazinyl, piperidinyl, pyrazolyl,
imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{10a} is selected from H, methyl, ethyl, propyl, butyl, OR¹⁴,
Cl, F, =O, NR¹⁵R¹⁶, CF₃, or phenyl substituted with 0-4
R^{10b};

R^{10b}, at each occurrence, is independently selected from H,
OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy,
propoxy, Cl, F, NR¹⁵R¹⁶, and CF₃;

Z is C₁-C₃ alkyl substituted with 1-3 R¹²;
C₂-C₃ alkenyl substituted with 1-3 R¹²;
C₂-C₃ alkynyl substituted with 1-3 R¹²;
C₆-C₁₀ aryl substituted with 0-4 R^{12b};
C₃-C₆ carbocycle substituted with 0-3 R^{12b}; or
5 to 6 membered heterocycle containing 1 to 4
heteroatoms selected from nitrogen, oxygen, and
sulphur, wherein said 5 to 6 membered heterocycle is
substituted with 0-3 R^{12b}; wherein said 5 to 6
membered heterocycle is selected from pyridinyl,
pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl,
pyrrolyl, piperazinyl, piperidinyl, pyrazolyl,
imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R¹², at each occurrence, is independently selected from
C₆-C₁₀ aryl substituted with 0-4 R^{12b};
C₃-C₆ carbocycle substituted with 0-3 R^{12b}; or

5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{12b}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{12b}, at each occurrence, is independently selected from H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R¹³, at each occurrence, is independently selected from H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, Cl, F, Br, CN, NR¹⁵R¹⁶, and CF₃;

R¹⁴ is H, phenyl, benzyl, methyl, ethyl, propyl, or butyl;

R¹⁵, at each occurrence, is independently selected from H, methyl, ethyl, propyl, and butyl;

R¹⁶, at each occurrence, is independently selected from H, OH, methyl, ethyl, propyl, butyl, benzyl, phenethyl, methyl-C(=O)-, ethyl-C(=O)-, methyl-S(=O)₂-, and ethyl-S(=O)₂-;

R¹⁷ is H, methyl, ethyl, propyl, butyl, methoxymethyl, ethoxymethyl, methoxyethyl, ethoxyethyl, phenyl substituted by 0-3 R^{17a}, or -CH₂-phenyl substituted by 0-3 R^{17a};

R^{17a} is H, methyl, methoxy, -OH, F, Cl, CF₃, or OCF₃;

R¹⁸, at each occurrence, is independently selected from

Amendment & Response – Docket No. DM-7076-A
Serial No.: 09/505,788
Date: April 10, 2002

H, methyl, ethyl, propyl, butyl, phenyl, benzyl, and
phenethyl; and

R¹⁹, at each occurrence, is independently selected from
H, methyl, and ethyl;

provided, when R¹³ is H,
then Z is C₂-C₃ alkenyl substituted with 1-3 R¹²; or
C₂-C₃ alkynyl substituted with 1-3 R¹².